The Long-Term Effects of Type 1 Diabetes Treatment and Complications on Health-Related Quality of Life

A 23-year follow-up of the Diabetes Control and Complications/Epidemiology of Diabetes Interventions and Complications cohort

OBJECTIVE—To examine the long-term effects of type 1 diabetes treatment, metabolic control, and complications on health-related quality of life (HRQOL).

RESEARCH DESIGN AND METHODS—A total of 1,441 participants, initially 13–39 years of age, were followed for an average of 23.3 years as part of the Diabetes Control and Complications Trial (DCCT) and the Epidemiology of Diabetes Interventions and Complications (EDIC) follow-up study. The Diabetes Quality-of-Life questionnaire (DQOL) was administered annually during DCCT and every other year during EDIC. Biomedical data, including HbA1c levels, exposure to severe hypoglycemia, intercurrent psychiatric events, and development of diabetes complications were collected at regular intervals throughout the follow-up.

RESULTS—Mean total DQOL scores were not significantly different between the former DCCT intensive and conventional treatment groups (DCCT baseline, 78 ± 8 vs. 78 ± 9; EDIC year 17, 75 ± 11 vs. 74 ± 11). Over the course of the study, a drop of ≥3 points in DQOL score from DCCT baseline maintained on two successive visits occurred in 755 individuals and was associated with increased HbA1c, albumin excretion rate, mean blood pressure, BMI, and occurrence of hypoglycemic events requiring assistance. Lower DQOL scores after 23.3 years of follow-up were associated with prior development of retinopathy (P = 0.0196), nephropathy (P = 0.0019), and neuropathy (P < 0.0001) as well as self-reported chest pain (P = 0.0004), decreased vision in both eyes (P = 0.0003), painful paresthesias (P < 0.0001), recurrent urinary incontinence (P = 0.0001), erectile dysfunction (P < 0.0001), and history of psychiatric events (P < 0.0001).

CONCLUSIONS—Among DCCT/EDIC participants, worsening metabolic control, serious diabetes complications and their associated symptoms, and development of psychiatric conditions led to decreased HRQOL.

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used as the principal quality-of-life outcome assessment during the DCCT and EDIC (2, 18, 19). It has now become a commonly used measure of patient perceptions of their quality of life with translation into multiple languages and use with a wide variety of patients (20).

In this article, we report on observations that have been made over an average of >23 years on the impact on HRQOL. We address three primary research questions: 1) does prior DCCT assignment to conventional therapy in comparison with intensive therapy adversely impact HRQOL? 2) does worse glycemic control or episodes of severe hypoglycemia adversely impact HRQOL? and 3) does the development of long-term, advanced complications of diabetes adversely impact HRQOL? In addition to these primary research questions, we also examined the association of HRQOL with psychiatric events and symptomatic manifestations of diabetes complications.

RESEARCH DESIGN AND METHODS

Study sample
Between 1983 and 1989, 1,441 participants with T1DM, 13–39 years of age, were enrolled in the DCCT. The DCCT consisted of two cohorts: the primary prevention cohort had diabetes for 1–5 years, no retinopathy, and urinary albumin excretion <40 mg/24 h, and the secondary intervention cohort had diabetes for 1–15 years, very mild to moderate nonproliferative retinopathy, and urinary albumin excretion ≤200 mg/24 h at baseline (18). Approximately one-half of the subjects (N = 711) were randomly assigned to intensive therapy, and the remainder (N = 730) were assigned to conventional therapy. The treatment groups maintained a separation of median 

HbA1c levels of ~2 percentage points (7.1 vs. 9.0%; 54.1 vs. 74.9 mmol/mol) during the 6.5-year average DCCT follow-up (18).

Since it had been shown to be highly effective in reducing diabetic microvascular complications, intensive therapy was recommended for all participants when the DCCT ended in 1993 (18, 19). Participants were then returned to their own health care providers for diabetes care. In 1994, 1,375 (96%) of the 1,428 surviving members of DCCT volunteered to participate in EDIC for annual observational follow-up (19). This report incorporates data through EDIC year 17 (2010), representing an average of 23.5 years of follow-up from randomization into DCCT. By EDIC year 17, 1,287 subjects continued to participate in EDIC, and of these, 1,177 (91%) completed the DQOL survey. Ninety-five participants had died by the end of EDIC year 17. For purposes of these analyses, two subjects with acute, temporary renal failure unrelated to diabetes were excluded.

Nonparticipants, including those who died, did not differ from participants in most characteristics at DCCT baseline including sex, age, education, blood pressure, and cholesterol. Nonparticipants had significantly higher 

HbA1c levels and a higher frequency of current cigarette smokers (Supplementary Table 1). Furthermore, 48% of participants were in the conventional treatment group compared with 61% of nonparticipants.

Quality-of-life assessment
The DQOL is a self-administered multiple-choice 46-item assessment that has been described in detail (15–17). The DQOL has four primary subscales (satisfaction, impact, diabetes worry, and social/vocational worry) that assess different aspects of quality of life. The scoring system yields scale scores that range from 0 (lowest quality of life) to 100 (highest quality of life), identical to the procedure for scoring the Medical Outcome Survey 36-item short-form health survey (SF-36) quality-of-life measure (21–23). Total DQOL scores are presented in the RESULTS section unless otherwise stated, and scores on the four subscales are presented in Supplementary Table 2.

Psychometric studies have indicated that the overall DQOL measure has excellent internal consistency (Cronbach α, 0.83–0.92) for both adults and adolescents (15–17). Test-retest reliability over an average period of 9 days was 0.92 for the overall measure (17). The DQOL has been shown to have convergent validity with conceptually relevant measures of well-being, psychiatric symptoms, and adjustment to illness (17). In addition, the DQOL discriminates between patients with different numbers of clinically evident complications (17) and is sensitive to different therapies for T2DM (17, 24, 25) and to a change in therapy for T1DM (i.e., pancreatic transplantation) (25). For this article, the primary outcome was the total DQOL score.

Past research has suggested that a difference of five points on the total DQOL score represents a clinically meaningful difference in HRQOL (15–17, 20, 24, 25). Consequently, this parameter was used in our longitudinal analyses of the effects of time-dependent predictors on change in quality of life. Specifically, an event was defined as a drop from baseline ≥5 points on two consecutive evaluations. We used a sustained decrease in DQOL score to confirm that a change occurred over a substantial time frame and was not transitory. We have used this same approach for other outcomes such as nephropathy, where a measure like albumin excretion rate (AER) can change up and down over time (26). The DQOL was administered annually throughout the DCCT and biannually during EDIC.

Biomedical evaluations and assessment of diabetes complications
The methods and scheduling of physical examinations, outcomes assessments, and laboratory measurements have been previously described in detail and remained consistent throughout DCCT and EDIC (18, 19, 26–28). During the DCCT (quarterly) and EDIC (annually), glycated hemoglobin values were measured in a central laboratory by high-performance liquid chromatography (18, 19). Retinopathy, assessed during EDIC years 11–14 by 7-field stereoscopic fundus photography according to the DCCT/EDIC protocol (26), was defined for these analyses as the presence of proliferative diabetic retinopathy (PDR) or worse, and/or a history of panretinal scatter-photon coagulation (laser) therapy. In addition, visual acuity (VA) was assessed to determine best corrected vision in the best and worst eye. Nephropathy was defined in this study as having any AER ≥300 mg/24 h through EDIC year 16 or end-stage renal disease (ESRD), defined as treatment with dialysis or transplantation for chronic renal failure (18, 19, 26). In EDIC years 13 to 14, board-certified nephrologists and electrolographers conducted neurological evaluations and electrophysiologic studies on all willing participants using the same protocol as was used in DCCT to determine the presence of clinical neuropathy (27, 28).

The occurrence of severe hypoglycemia was documented quarterly during the DCCT and within 3 months of the annual visit during EDIC. It was defined in two ways: 1) any event requiring the
assistance of another person, with either a blood glucose <50 mg/dL (2.78 mmol/L) and/or subsequent reversal of symptoms with oral carbohydrate, subcutaneous glucagon, or intravenous glucose; or 2) the same criteria plus unconsciousness, seizure, or coma (18,29). Twenty-seven percent of severe hypoglycemic episodes involved coma or seizure (30). In this article, the episodes of severe hypoglycemia requiring assistance and those also resulting in seizure or coma were analyzed separately.

Symptomatic data and changes since the last annual visit were self-reported each year during EDIC for the following symptoms: chest pain, decreased vision, paresthesias in hands/feet, recurrent urinary incontinence, and impotence.

### Intercurrent psychosocial events and psychiatric symptoms

Information about intercurrent psychosocial events and psychiatric history was reported quarterly during the DCCT and annually during EDIC based on subject interviews. Information about education level, marital status, psychiatric treatment, psychiatric hospitalization, and suicide attempts was documented. A psychiatric event was defined as at least one occurrence in EDIC accompanied by inpatient or outpatient treatment for any psychiatric event during the same year.

#### Statistical analyses

Demographic and clinical characteristics were compared using the Wilcoxon rank-sum test to evaluate treatment group differences for ordinal and numeric variables (31). The contingency χ² test was used for categorical variables; when the sample size was small, the Fisher exact test was used (31).

Cox proportional hazard models were used to determine the effects of demographic and biomedical assessments on the risk of a sustained five-point drop in total DQOL over two consecutive assessments during DCCT and EDIC. Each characteristic was modeled separately as a time-dependent covariate adjusting for its baseline value as well as sex, baseline age, and baseline mean years of education. Since QOL was only measured during odd years in EDIC, each model was stratified for calendar year of randomization, allowing subjects who entered into the study during the same calendar year to have the same visit sequence. Updated mean values are time-weighted, running means up to each study visit in the DCCT and EDIC.

Separate ANCOVA models were used to assess the relationship between total DQOL and both complication status and functional symptoms by year 17 of EDIC. Adjustments were made for sex, baseline age, baseline mean years of education, and baseline DQOL score. Least square means and SEs were compared for participants with and without the characteristic or complication of interest. Statistical analyses were performed using the SAS V

### Table 1—Characteristics of participants who completed the DQOL in EDIC year 17

| Characteristic                  | DCCT baseline (1983–1989) | EDIC year 17 (2010) |
|--------------------------------|---------------------------|---------------------|
|                                | Intensive (N = 606)       | Conventional (N = 569) |
|                                | Intensive (N = 606)       | Conventional (N = 569) |
| Sex (% female)                 | 48.2                      | 46.2                |
| Race (% white)                 | 96.2                      | 96.8                |
| Mean age (years)               | 27.3 ± 7.1                | 26.6 ± 6.9          |
| College graduate (%)†          | 45.6                      | 47.4                |
| Married or remarried (%)†      | 59.9                      | 63.2                |
| Professional or technical occupation (%)† | 38.0       | 39.9                |
| Current cigarette smoker (%)   | 20.8                      | 18.1                |
| Current drinker (%)            | 21.3                      | 22.7                |
| Duration of diabetes (years)   | 5.8 ± 4.2                 | 5.5 ± 4.1           |
| HbA1c (%)‡                     | 9.1 ± 1.6                 | 8.9 ± 1.5           |
| HbA1c (mmol/mol)‡              | 75.5 ± 17.4               | 73.8 ± 16.9         |
| Retinopathy (%)                | 51.5                      | 49.0                |
| PDR or worse (%)^              | 0                         | 0                   |
| AER >300 mg/24 h or ESRD (%)^‡ | 0                         | 0                   |
| Confirmed clinical neuropathy (%)# | 6.8          | 5.6                |
| Blood pressure                 |                           |                     |
| Systolic (mmHg)                | 113.3 ± 11.7              | 115.2 ± 11.9**      |
| Diastolic (mmHg)               | 72.4 ± 8.9                | 73.1 ± 8.6          |
| Hypertension (%)               |                           | 72.3 ± 9.3          |
| Lipids                         |                           | 65.3                |
| Cholesterol (mg/dL)            | 177.7 ± 33.4              | 173.8 ± 32.9        |
| LDL cholesterol (mg/dL)        | 111.0 ± 29.3              | 108.1 ± 29.1        |
| Hypercholesterolemia (%)       |                           | 97.3 ± 30.2         |
| Total quality of life          | 77.8 ± 8.5                | 77.9 ± 8.2          |

Data are means ± SDs or percent. *P < 0.05, **P < 0.01 for treatment group differences comparing intensive vs. conventional at each time point separately by the Wilcoxon rank-sum test for ordinal and numeric variables or the contingency χ² for categorical variables. †Percentages at DCCT baseline were calculated among adults (≥21 years) only (N = 945). ‡DCCT baseline is eligibility value. ^PDR or worse at DCCT baseline or EDIC year 11-14 visit. §Any AER >300 mg/24 h or ESRD at DCCT baseline or up through EDIC year 16. #Confirmed clinical neuropathy at DCCT baseline or EDIC year 13/14. ‖Data were not collected in DCCT. Hypertension is defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, documented hypertension, or the use of antihypertensive agents for the treatment of hypertension. Hypercholesterolemia is defined as LDL cholesterol ≥130 mg/dL or the use of lipid-lowering agents.
HRQOL and diabetes treatment and complications

9.2 statistical analysis software (SAS Institute, Cary, NC).

RESULTS

Clinical characteristics of the participants
There were no significant differences between treatment groups in demographic or clinical characteristics at baseline, other than a clinically insignificant difference in systolic blood pressure (Table 1). At the 17-year EDIC follow-up, after an average of 23.5 years, 66% of all DCCT/EDIC participants had developed hypertension, 65% hypercholesterolemia, and 19% proliferative diabetic retinopathy or worse. The lower prevalence of retinopathy and nephropathy in the former intensive treatment group at EDIC year 17 reflects the previously published salutary effects of intensive therapy (19).

Impact of prior treatment group assignment on HRQOL
No differences in total DQOL or DQOL subscale scores were found between the intensive and conventional groups at any time points. Mean total DQOL scores were not significantly different between the former DCCT intensive and conventional treatment groups at baseline (78 ± 8 vs. 78 ± 9), DCCT closeout (78.1 ± 8.8 vs. 78.2 ± 9.4), or EDIC year 17 (75 ± 11 vs. 74 ± 11). The group as a whole did not show a significant trend for decreasing DQOL scores over time (Table 1 and Supplementary Table 2).

There were 755 (52%) DCCT/EDIC participants who had a DQOL event (defined as a decrease in DQOL from baseline of ≥5 points on two consecutive evaluations) by EDIC year 17, with 293 (39%) occurring during DCCT and 462 (61%) during EDIC. There were no significant treatment group differences (P = 0.9339). Compared with females, males had a 13.8% lower risk of reaching a DQOL end point (hazard ratio 0.862 [95% CI 0.744–0.999]; P = 0.0484).

Impact of glycemic control and hypoglycemic episodes on HRQOL
Higher values of HbA1c, log(AER), mean blood pressure, and BMI were all associated with a sustained drop of ≥5 points in DQOL score, before and after adjustment for sex, age, and mean years of education at DCCT baseline (Table 2). Subjects who experienced severe hypoglycemic events had a 36% higher risk of having a ≥5-point decrease in DQOL than those without such events. Analyses using the more stringent definition of severe events that included those that led to unconsciousness, coma, or seizure did not reveal an impact on DQOL scores. The effects of hypoglycemia, HbA1c, and BMI were significant even after adjustments of other covariates including log(AER) and mean blood pressure (Table 2).

Impact of advanced complications on HRQOL
Development of advanced stages of retinopathy (P = 0.0196), nephropathy (P = 0.0019), and confirmed clinical neuropathy (P < 0.0001) were associated with lower total DQOL scores at year 17 of EDIC (an average of 23.5 years of follow-up), after adjusting for sex, age, and mean years of education at baseline (Table 3). There was a significant effect of the development of any complications (none vs. one or more) (P = 0.0009), with a linear trend showing that those subjects with all three complications had the lowest DQOL.
score of 71.6 ± 0.7 compared with no complications (P < 0.0001) (Table 3). By EDIC year 17, 13 subjects had chronic renal failure due to diabetes and were treated with either dialysis or transplantation. Their mean adjusted quality-of-life score was 74.6 ± 2.7.

### Relationship of self-reported symptoms and HRQOL

Self-reported symptoms associated with these complications at year 17 were also linked to decreased DQOL scores (Table 4). Specifically, chest pain (P = 0.004), decreased vision in both eyes (P = 0.0005), paresthesias in hands or feet (P < 0.0001), urinary incontinence (P = 0.0001), and male erectile dysfunction (P < 0.0001) were associated with lower EDIC year 17 DQOL scores, after adjusting for sex, baseline age, baseline mean years of education, and baseline DQOL score. Among both men and women, increasing number of symptoms was associated with a lower DQOL score (men, P = 0.0091; women, P = 0.0028). Because the principal DCCT end point was progressive retinal disease, we also compared DQOL scores for participants at different levels of VA. The 14 participants with VA worse than 20/100 in the worse eye had a mean total DQOL score of 68.5 ± 7.9 compared with 74.9 ± 10.5, 74.6 ± 10.7, and 76.0 ± 12.5 for VA better or equal to 20/20, 20/20 to 20/40, and 20/40 to 20/100, respectively (P = 0.0661).

### Relationship of psychiatric events and HRQOL

Self-reported history of treated anxiety (P < 0.0001) and treated depression (P < 0.0001) were also associated with lower DQOL scores (Table 4). Two hundred subjects reported both anxiety and depression, and their mean adjusted quality-of-life score was 69.2 ± 0.7. Only a small number of participants were ever hospitalized for a psychiatric illness or reported suicidal attempts (27 attempts in 18 individuals), and both were associated with decreased DQOL scores (P < 0.0001). An increasing number of psychiatric events was reflected in a decreased DQOL score (P < 0.0001).

### CONCLUSIONS

We present the longest prospective follow-up study of HRQOL in individuals with T1DM and describe their course of quality-of-life experiences over ~25 years. The therapy applied to the intensive treatment group during DCCT and encouraged for the entire cohort during the 17 years of EDIC follow-up has resulted in relatively low rates of severe diabetes complications.

Our findings support a salutary effect of the prevention and delay of complications on HRQOL (18,26–28,30,32). Decreases in HRQOL are particularly likely among patients with a higher prevalence of severe complications.

With regard to our first research question and consistent with our previous report at the end of the DCCT, there are no apparent adverse effects of intensive therapy on HRQOL (2). With regard to our second research question and in contrast to our initial HRQOL report based on an average of 6.5 years of treatment during DCCT (2), after an additional 17 years of follow-up, we now find an association between elevated HbA₁c levels and severe hypoglycemia requiring assistance and a sustained decrease in DQOL scores.

With regard to our third research question, the development of advanced complications and the symptoms resulting from these complications, such as decreased VA, erectile dysfunction, and incontinence, were associated with decreases in HRQOL. Each of the three complications assessed (retinopathy, neuropathy, and nephropathy) were individually associated with lower DQOL scores in comparison with those without the complication; moreover, using a composite index, increasing numbers of advanced complications led to lower quality of life. Consistent with the assessment of complications, functional symptoms were also associated with lower quality of life. It is important to note that while almost all patients developed some degree of retinopathy (88% prior intensive group; 96% prior conventional group) and 19% required laser treatment or vitreoretinal surgery in at least one eye, only 4.8% (N = 52) had best corrected vision worse than 20/40 in one eye, and only 13 had best corrected vision worse than 20/100 in one eye. Patients with best corrected vision less than 20/100 in their worse eye had lower HRQOL than those with better VA.

Finally, the development of common psychiatric syndromes like depression is linked to HRQOL (5). This relationship was seen in the association of psychiatric conditions and their treatment on lower DQOL scores after an average of 23.5 years of follow-up.

The current study has unique strengths compared with previous studies of T1DM, including its long-term, consistent follow-up of a large cohort; detailed demographic and clinical information

### Table 3—Medical complications by total DQOL score at EDIC year 17 after an average of 23.5 years of follow-up

| Complications | N  | Total DQOL score at EDIC year 17 | P value |
|---------------|----|---------------------------------|---------|
| Retinopathy   |    |                                 |         |
| No            | 956| 74.8 ± 0.3                      | 0.0196  |
| Yes           | 219| 73.1 ± 0.7                      |         |
| Nephropathy   |    |                                 |         |
| No            | 1,061| 74.8 ± 0.3                      | 0.0019  |
| Yes           | 114 | 71.8 ± 0.9                      |         |
| Neuropathy    |    |                                 |         |
| No            | 780 | 75.5 ± 0.3                      | <0.0001 |
| Yes           | 314 | 72.7 ± 0.5                      |         |

Data are least square means ± SEs, unless otherwise indicated, adjusted for sex, baseline age, baseline mean years of education, and baseline quality-of-life score. Sample sizes vary due to the availability of data at the annual visit. *Retinopathy is defined as any proliferative diabetic retinopathy or worse at EDIC year 11–14 visit; nephropathy is defined as having any AER ≥300 mg/24 h or ESRD up through EDIC year 16; and neuropathy is defined as confirmed clinical neuropathy at EDIC year 13/14. **P value corresponding to zero vs. one complication and zero vs. two or more complications.
HRQOL and diabetes treatment and complications

Table 4—Self-reported functional status and history of psychiatric events occurring in EDIC by total DQOL score at EDIC year 17 after an average of 23.5 years of follow-up

| | N | Total DQOL score at EDIC year 17 | P value |
|---|---|---------------------------------|---------|
| Self-reported functional status | | | |
| Cardiovascular symptoms | | | |
| Chest pain | | | |
| No | 1,132 | 74.7 ± 0.3 | 0.0004 |
| Yes | 43 | 69.3 ± 1.5 | |
| Ophthalmic symptoms | | | |
| Changes in vision | | | |
| No eyes | 905 | 75.1 ± 0.3 | |
| One eye | 50 | 72.0 ± 1.4 | 0.0293† |
| Both eyes | 218 | 72.5 ± 0.7 | 0.0005 |
| Neurologic symptoms | | | |
| Paresthesias in hands/feet | | | |
| No | 784 | 76.2 ± 0.3 | <0.0001 |
| Yes | 389 | 71.1 ± 0.5 | |
| Recurrent urinary incontinence | | | |
| No | 987 | 75.0 ± 0.3 | 0.0001 |
| Yes | 183 | 71.8 ± 0.8 | |
| Impotence* | | | |
| No | 412 | 75.5 ± 1.5 | <0.0001 |
| Yes | 215 | 71.3 ± 1.6 | |
| No. of self-reported symptoms for males | | | |
| Zero | 34 | 77.8 ± 1.6 | 0.0091 |
| One | 341 | 76.7 ± 0.5 | |
| Two | 237 | 74.2 ± 0.6 | |
| Three | 8 | 72.7 ± 3.3 | |
| No. of self-reported symptoms for females | | | |
| Zero | 30 | 75.2 ± 1.8 | 0.0028 |
| One | 300 | 73.9 ± 0.6 | |
| Two | 213 | 72.3 ± 0.7 | |
| Three | 12 | 64.4 ± 2.8 | |
| History of psychiatric events** | | | |
| Nervousness or anxiety | | | |
| No | 943 | 75.6 ± 0.3 | <0.0001 |
| Yes | 231 | 69.9 ± 0.6 | |
| Affective disorder | | | |
| No | 873 | 76.0 ± 0.3 | <0.0001 |
| Yes | 301 | 70.2 ± 0.6 | |
| Suicidal attempt | | | |
| No | 1,156 | 74.7 ± 0.3 | <0.0001 |
| Yes | 18 | 61.6 ± 2.3 | |
| Psychiatric hospitalization or outpatient treatment that included use of psychiatric medications | | | |
| No | 1,049 | 75.0 ± 0.3 | <0.0001 |
| Yes | 125 | 70.1 ± 0.9 | |
| No. of psychiatric events | | | |
| Zero | 834 | 76.0 ± 0.3 | <0.0001 |
| One | 102 | 73.4 ± 0.9 | |
| Two | 149 | 70.5 ± 0.8 | |
| Three | 75 | 69.9 ± 1.1 | |
| Four | 14 | 60.3 ± 2.5 | |

Data are least square means ± SEs, unless otherwise indicated, adjusted for sex, baseline age, baseline mean years of education, and baseline QOL score. Sample sizes vary due to the availability of data at the annual visit.

*Among men only (N = 627). **Psychiatric events were self-reported annually in EDIC. An event was defined as at least one occurrence in EDIC accompanied by inpatient or outpatient treatment for any psychiatric event that same year. †P value corresponding to no eyes vs. one eye and no eyes vs. both eyes.

collected prospectively using standardized methods from relatively early in the course of illness; repeated measurement of HRQOL; the diversity of clinical outcomes; and the wide range of ages represented during the study period (13–65 years of age).

The study also has limitations that can affect the generalizability of its findings. These include the selection and self-selection of participants to enroll in a randomized clinical trial that required careful screening and adherence to a complex regimen over an extended period of time. Such patients have relatively high levels of motivation compared with the general population. Moreover, potential participants with psychosocial problems and limited social support would have been screened out. The DCCT/EDIC cohort had relatively high average socioeconomic status and education level of the group and was predominantly Caucasian. During DCCT, there was a high degree of assistance provided by the study nurse-coordinators and physicians. This was especially evident for the intensively treated group during DCCT. Such factors would tend to lessen the impact on HRQOL, so these findings may underestimate the effects in typical clinical populations, who also may have higher rates of severe complications.

Although our cohort, and in particular the intensive treatment group, received an unusual level of attention and support during the 6.5 years of the DCCT, during 17 of the average of 23.5 years represented by this study, the participants have been followed in typical practice settings with less support from the study. The return to usual care settings may increase the representativeness of this group of T1DM patients.

Our ability to examine the effects of treatment assignment, exposure to varying levels of glycemia, including severe hypoglycemia, and the development of medical complications provide a benchmark for comparison with other research studies and with patients followed in typical clinical settings. We have constructed a quantitative picture of the impact of different interventions, levels of metabolic control, and complications on patient experiences of illness. Smaller studies that have explored in greater depth the experiences of illness using qualitative methods augment these findings while evaluating specific aspects of illness (33). Other studies, typically cross-sectional or of shorter duration, but with
broader representation of patient types, have provided information that is reasonably consistent with our findings. Specifically, complications exert a stronger effect on HRQOL than diabetes management approaches. Moreover, as in our study, intensification of treatment using multiple daily injections and insulin pumps does not lead to decreased quality of life (1,7,11,12,13). Indeed, intensive treatment and the subsequent reduction of symptomatic complications helps maintain the long-term quality of life of patients with diabetes.

The information derived from studies like this one can be useful for clinicians as the initiate newly diagnosed patients into treatment and work with patients collaboratively over time. Indeed, such personal experiences are increasingly viewed as critical for patients in making their own therapeutic decisions (34,35) and engaging their clinical care team in dealing with the rigors of long-term diabetes. Moreover, symptoms related to sexual and urologic functions may be embarrassing for patients to discuss, and engaging their clinical care team in collaborative over time. Indeed, such

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A.M.J. wrote the manuscript. B.B.H. researched the data, performed analyses, and contributed to writing the manuscript. P.A.C. researched the data and contributed to writing the manuscript. R.A.G.-K. and M.E.L. contributed to writing the manuscript. A.M.J. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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The information derived from studies like this one can be useful for clinicians as the initiate newly diagnosed patients into treatment and work with patients collaboratively over time. Indeed, such personal experiences are increasingly viewed as critical for patients in making their own therapeutic decisions (34,35) and engaging their clinical care team in dealing with the rigors of long-term diabetes. Moreover, symptoms related to sexual and urologic functions may be embarrassing for patients to discuss, but have distinct impact on patient experience of illness and represent an important area for inquiry by treating health care professionals.
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