Relationship of Urologic Complications With Health-Related Quality of Life and Perceived Value of Health in Men and Women With Type 1 Diabetes: The Diabetes Control and Complications Trial/Epidemiology of Interventions and Complications (DCCT/EDIC) Cohort

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OBJECTIVE

Limited information exists about the influence of urologic complications on health-related quality of life (HRQOL) in patients with type 1 diabetes.

RESEARCH DESIGN AND METHODS

We studied 664 men and 580 women from the Diabetes Control and Complications Trial/Epidemiology of Interventions and Complications Study: mean ages were 51.6 ± 6.6 and 50.6 ± 7.2 years and duration of diabetes was 29.5 ± 4.8 and 29.8 ± 5.1 years, respectively. We assessed associations of sexual dysfunction, lower urinary tract symptoms (LUTS), and, in women, urinary incontinence (UI) with general quality of life (SF-36), perceived value of health (EuroQol-5), diabetes-related quality of life (Diabetes Quality of Life Scale [DQOL]), and psychiatric symptoms (Symptom Checklist 90-R).

RESULTS

In both men and women, urologic complications adversely affected HRQOL and psychiatric symptoms, even after accounting for history of depression leading to treatment. Multivariable analyses accounting for the presence of diabetic retinopathy, neuropathy, and nephropathy also revealed substantial independent effects. In men, for example, the odds (95% CI) of a low DQOL score (≤25th percentile) were 3.01 (1.90–4.75) times greater with erectile dysfunction and 2.65 (1.68–4.18) times greater with LUTS and in women, 2.04 (1.25–3.35) times greater with sexual dysfunction and 2.71 (1.72–4.27) times greater with UI/LUTS combined compared with men and women without such complications. Similar effects were observed for the other measures.

CONCLUSIONS

Sexual dysfunction and urinary complications with type 1 diabetes are associated with decreased quality of life and perceived value of health and with higher levels of psychiatric symptoms, even after accounting for other diabetes complications and depression treatment.

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Type 1 diabetes leads to the development of numerous serious and life-threatening complications. Many studies have examined the influence of retinopathy, neuropathy, and nephropathy on patient reports of their health-related quality of life (HRQOL) (1–6). Although urologic complications occur commonly in patients with diabetes and have been found to adversely affect HRQOL in other populations (7), few studies have specifically examined the influence of diabetes-related urologic disease on HRQOL (8,9). These studies primarily assessed men with type 2 diabetes (8,9). The relationship between urologic disease and HRQOL in men or women with type 1 diabetes has not been established. Moreover, to what extent such urologic complications affect HRQOL in the presence of other debilitating complications of type 1 diabetes is not clear.

The Diabetes Control and Complications Trial (DCCT) and its observational follow-up, the Epidemiology of Diabetes Intervention and Complications (EDIC) study, have been studying a large cohort of participants with type 1 diabetes for an extended period. Assessments of urologic complications, HRQOL, perceived value of health, and psychiatric symptoms were performed at year 17 of EDIC (an average of 23.5 years after initiation of the DCCT). We addressed two research questions:

Are urologic complications, including lower urinary tract symptoms, urinary incontinence, and sexual dysfunction, associated with decreased general and illness-specific HRQOL, perceived value of health, and higher psychiatric symptom levels?

Do urologic complications independently influence HRQOL, perceived value of health, and psychiatric symptom levels, even after accounting for the effects of nephropathy, neuropathy, and retinopathy?

RESEARCH DESIGN AND METHODS

Study Sample

Between 1983 and 1989, 1,441 participants with type 1 diabetes, 13 to 39 years of age, were enrolled in the DCCT (10); of these, 711 subjects (49.3%) were randomly assigned to intensive therapy (3 or more insulin injections daily or subcutaneous infusion with external pump, guided by self-glucose monitoring). The treatment groups maintained a separation of HbA_{1c} levels of about 2 percentage points (7.1% vs. 9.0% [54 mmol/mol vs. 75 mmol/mol]) during the 6.5 average years of DCCT follow-up.

Intensive therapy was recommended for all participants when the DCCT ended in 1993 (10,11). Participants returned to their own health care providers for ongoing diabetes care. In 1994, 1,375 of the 1,428 surviving members of DCCT (96%) volunteered to participate in the EDIC study for annual observational follow-up (11). In year 17 of EDIC, subjects were invited to participate in UroEDIC, an ancillary study of urologic complications that included assessments of these complications and measures of HRQOL done at that annual visit. The results presented in this report are based on those assessments at year 17.

Assessment of Urologic Complications

Erectile dysfunction (ED) was assessed in men using the International Index of Erectile Function (IIEF), a reliable, validated instrument used widely in clinical trials and epidemiologic surveys (12). For these analyses, our definition of ED and primary ED outcome was based on responses to a single item proxy from the IIEF, question 15, which asks the following: "Over the past 4 weeks, how would you rate your confidence that you get and keep your erection?" Participants who answered "very low" (1) or "low" (2) were considered to have ED, and those who answered "moderate" (3), "high" (4), or "very high" (5) were considered to have no ED. This single-item definition of ED has been shown to strongly correlate with total erectile function domain scores (Spearman r = 0.77, $P < 0.001$) and, among IIEF items, has the highest correlation with sexual bother scores (13). Using the single item also has the benefit of allowing assessment of ED in the entire cohort regardless of sexual activity and presence or absence of a partner.

Sensitivity analyses were conducted using the entire IIEF. For purposes of the primary analyses presented in this report, men who used medications to successfully treat ED were not considered to have current ED. We performed additional analyses using the single confidence in erection question by categorizing men into four separate groups: *1*) no ED; *2*) ED that is treated with subject reporting no current problem with confidence getting an erection; *3*) treated ED, but reporting current problem with confidence getting an erection; *4*) not being treated and reporting current problem with confidence getting an erection. This was done to examine the specific effect of currently symptomatic ED on HRQOL.

Lower urinary tract symptom (LUTS) severity was assessed in men and women with the American Urological Association Symptom Index (AUASI), which has been validated in both men and women (14,15). The AUASI includes a standardized seven-item questionnaire that quantifies the presence and frequency of the following lower urinary tract symptoms: nocturia, frequency, urgency, weak urinary stream, intermittency, straining, and the sensation of incomplete emptying. Scores range from 0 to 35. Using widely accepted cut points of 0–7, 8–19, and 20–35 designated as none/mild, moderate, and severe LUTS, respectively, we divided participants into those with none/mild LUTS versus those with moderate and severe LUTS (14).

Sexual dysfunction was assessed in women using the Female Sexual Function Index-reduced (FSFI-R) (16,17), an abbreviated validated version of the FSFI that assesses sexual function across six domains, including sexual desire, arousal, lubrication, orgasm, satisfaction, and pain. The FSFI-R uses 7 of the 19 items from the FSFI. The items are 5-point Likert-type items. Unlike the full FSFI, higher scores on the FSFI-R reflect worse sexual functioning. The FSFI-R total score is the sum of all the items representing each sexual function domain added with the mean score of the satisfaction items. Sexual dysfunction is defined as FSFI-R $\geq$22.75.

Urinary incontinence (UI) was assessed in women with a questionnaire based on validated instruments used in previous studies (18). The sequence of incontinence questions begins with "During the past 12 months how often have you leaked even a small amount of urine. . ." Frequency of incontinence is ascertained as every day, one or more times per week, one or more times per month, or less than once per month.

Among women with weekly UI, type of incontinence is classified by the addition of questions "...during activities like coughing, sneezing, lifting, or exercise?" (stress incontinence) and "...with an urge to urinate and couldn't get to the bathroom fast enough?" (urge incontinence). Severity of incontinence is determined based on incontinence frequency and amount of urine lost per episode (drops, small splashes, more) using the validated Sandvik Severity score (18), which is calculated as the product of frequency and amount of urine loss scores on a scale of 1–12. We used as a cutoff those with none/mild UI (1–2) versus those with moderate to severe UI (≥3). On the basis of findings from the Boston Area Community Health (BACH) study (7), we combined LUTS and UI into a single outcome representing urinary symptoms for our analyses of women.

Quality of Life

The SF-36 (19,20) was designed for use in clinical practice and research and is designed as a general measure that can be used for individuals with a wide range of conditions. It consists of eight scales that address *1*) Physical Function, *2*) Social Function, *3*) limitations in physical role, *4*) Bodily Pain, *5*) Mental Health, *6*) limitations in emotional role, *7*) Vitality, and *8*) General Health Perception. Linear transformations of scores to a mean of 50 and SD of 10, based on norms from the general U.S. population, yield the same mean and SD for all eight scales. These scales are commonly used to present results. A 5-point difference in scores is considered clinically relevant (19,20).

Perceived value of health or health utility was measured by the EuroQol-5D (EQ-5D), a standardized instrument used to measure health outcomes applicable to a wide range of health conditions and treatments (21,22). EQ-5D is cognitively simple, and self-completion takes only a few minutes. This instrument provides a descriptive profile that classifies respondents into 1 of 243 distinct health states based on the five dimensions of mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, each with three levels (no, moderate, or extreme health problems). A scoring algorithm is used to assign an EQ-5D index score to self-reported health states from a set of population-based preference weights, with 1.0 representing perfect health and 0 representing death (21,22).

Diabetes-Specific Quality of Life

The Diabetes Quality of Life Measure (DQOL) is a self-administered multiple-choice 46-item assessment that has been described in detail (23,24). In addition to a total score, the DQOL has four primary subscales (satisfaction, impact, diabetes worry, and social/vocational worry). As with the SF-36, the scoring system yields scale scores that range from 0 (lowest quality of life) to 100 (highest quality of life) (19,20). Psychometric studies have indicated that the DQOL measure has excellent internal consistency (Cronbach α = 0.83–0.92), test-retest reliability, and validity (23,24). In addition, the DQOL is sensitive to different therapies for diabetes (3,24) and to a change in therapy for type 1 diabetes (3). A 5-point difference in the total DQOL score is considered to be clinically significant (3). The DQOL was administered annually throughout the DCCT and biannually during EDIC and was given as part of the UroEDIC study.

Psychiatric Symptoms

Psychiatric symptoms were assessed using the Psychiatric Symptom Checklist 90-R (SCL-90R), a widely used and well-validated measure that provides an assessment of psychiatric symptoms and generates a total score on the global severity index (GSI) and subscales, including depression (25). T scores are derived from normative samples. Higher scores reflect more symptoms. A score of ≥63 for the total SCL90R GSI is considered to reflect the likely presence of a current psychiatric condition and so was applied as a cutoff in our analyses.

Biomedical Evaluations and Assessment of Diabetes Complications

The methods and scheduling of assessments during DCCT and EDIC have been described in detail and have remained consistent throughout (1,11,26–28). During the DCCT and EDIC, HbA_{1c} values were measured quarterly and annually, respectively, in a central laboratory by high-performance liquid chromatography (10).

Retinopathy, assessed during EDIC years 11–14 by seven-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-photocoagulation (laser) therapy. Nephropathy was defined as having any albumin excretion rate (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 (10,11). In EDIC years 13–14, neurologic evaluations and electrodiagnostic studies were conducted using the same protocol as was used in DCCT. Confirmed clinical neuropathy was defined as a combination of the presence of signs and symptoms consistent with distal symmetric polyneuropathy based on an examination by a board-certified neurologist and nerve conduction studies with abnormal results (27,28).

Statistical Analyses

Demographic and clinical characteristics were compared using the Wilcoxon rank sum test to evaluate treatment group differences for ordinal and numeric variables (29). The contingency χ^2 test was used for categorical variables.

Results for men and women were examined separately, with ANCOVA models used to assess the relationship between urologic complication status and HRQOL scores at year 17 of EDIC. Adjustments were made for EDIC year 17 age and education. These analyses were repeated with further adjustment for history of diagnosis and treatment for depression. Least square means and SEs were compared for participants with and without the urologic complication of interest.

Multivariable logistic regression models were used to estimate the odds of a low HRQOL score (≤25th percentile for the SF-36 scales, EQ-5D, and DQOL) and high level of psychiatric symptoms (SCL-90R GSI score ≥63) by urologic complication status. For men, participants with no urologic complications were compared with those with ED only, LUTS only, and both ED and LUTS. For women, participants with no urologic complications were compared with those with female sexual dysfunction (FSD) only, UI and/or LUTS only, and FSD plus UI

and/or LUTS combined. Additional multivariable logistic models assessed the simultaneous effects of urologic complications and microvascular complications in men and women separately. All logistic regression models were adjusted for DCCT treatment group assignment, EDIC year 17 age and education, and DCCT/EDIC time-weighted HbA_{1c}. Interactions between time-weighted HbA_{1c} and each of the urologic complications were evaluated in final models presented in Tables 3 and 4. We also categorized male participants into four groups based on current confidence in getting an erection and whether they were currently being treated for ED and examined the effects on HRQOL. Additional analyses were done using the total IIEF score instead of the single ED confidence question. Statistical analyses were performed using SAS 9.2 statistical analysis software (SAS Institute Inc., Cary, NC).

RESULTS

This report incorporates data from EDIC year 17, an average of 23.5 years after randomization into DCCT, on 1,224 subjects (644 men; 580 women) who agreed to participate in the UroEDIC ancillary study (96% of eligible men; 94% of eligible women). Except for the clinical characteristics deriving from treatment effects of assignment to intensive therapy during DCCT, the prior intensive and conventional groups were quite similar (Table 1). Forty-nine percent of participants came from the DCCT conventional treatment group. Nonparticipants, including those who died, did not differ from participants on most characteristics at DCCT baseline, including sex, age, education, and blood pressure. Nonparticipants had significantly higher HbA_{1c} levels and cholesterol levels and a higher frequency of current cigarette use.

Currently symptomatic ED was reported by 31% of participating men. An additional 15% used medications to treat ED and did not report current symptoms. Sexual dysfunction was reported by 26% of women. Moderate/severe LUTS was reported by 25% of men and 22% of women. Moderate/severe UI was reported by 30% of women. Women had significantly lower scores than men on the HRQOL measures, with the exception of the single item question from the SF-36 addressing global health perception (data not shown). For example, for men and women, respectively, the total DQOL score was 75.9 $\pm$ 11.0 vs. 73.3 $\pm$ 10.6 ($P < 0.0001$), the EQ-5D score was 0.89 $\pm$ 0.14 and 0.86 $\pm$ 0.16 ($P < 0.0009$), and the SF-36 Physical Function score was 87.5 $\pm$ 19.1 vs. 82.3 $\pm$ 22.7 ($P < 0.0001$). The SCL90-R GSI score was higher in women than in men: 52.1 $\pm$ 12.1 vs. 49.3 $\pm$ 10.7 ($P < 0.0001$). The GSI scores in 79 women (14%) and 59 men (9%) were $\geq$63.

Prevalent ED and moderate/severe LUTS in men were associated with significantly lower HRQOL and perceived value of health and with a higher level of psychiatric symptoms on all measures after adjusting for age and education. FSD and moderate/severe LUTS and/or UI in women were also associated with lower HRQOL and perceived value of health and with a higher level of psychiatric symptoms after adjusting for age and education (Table 2). In year 17, 19% of men (n = 124) and 33% of women (n = 184) reported a history of diagnosis of depression that resulted in outpatient or inpatient treatment. When the means reported in Table 2 were further adjusted for a history of depression that resulted in treatment, all comparisons remained statistically significant at the same levels, with the exception of the effect of ED versus no ED on SF-36 Role Function Emotional in men and FSD versus no FSD on SF-36 Social and Role Function in women (see footnote in Supplementary Table 1). The differences found in these comparisons were substantial; in almost all comparisons with the DQOL and SF-36, the differences in mean values exceeded the previously determined minimally clinically significant difference of 5 points (3,19,20). In addition, when subjects were compared using the SCL-90R cutoff score (GSI $\geq$63), men and women with ED, FSD, LUTS for men, and LUTS/UI combined for women were more likely than those without these conditions to have high GSI scores: 15.5% vs. 6.6% for ED, 18.4% vs. 6.2% for male LUTS, 21.9% vs. 10.3% for FSD, and 21.0% vs. 8.5% for female LUTS/UI combined ($P < 0.001$ for all 4 comparisons).

We also examined whether having both sexual dysfunction and LUTS in men (and LUTS and UI combined in women) adversely affected HRQOL, perceived value of health, and psychiatric symptoms above having either complication separately. Among men, the odds of having a low HRQOL or perceived value of health score ($\leq$25th percentile) and high psychiatric symptom level (SCL-90R GSI score $\geq$63) were consistently found for ED only and LUTS only, and the odds ratios were higher when both complications were present. Among women, sexual dysfunction only and UI/LUTS only were also consistently associated with higher odds of low HRQOL and perceived value of health and high psychiatric symptom level. However, unlike men, the odds of having decreased HRQOL-related outcomes did not typically increase when both sets of complications were present in women (Table 3). All analyses presented in Table 3 were adjusted for DCCT treatment group assignment, EDIC year 17 age and education, and DCCT/EDIC time-weighted HbA_{1c}. Furthermore, no interactions between time-weighted HbA_{1c} and any urologic complication were found.

Multivariable analyses, in which retinopathy, neuropathy, and nephropathy were entered simultaneously along with each urologic complication, also showed significant independent effects for the urologic complications. Among both men and women, the urologic complications were, in all but one analysis, independent predictors of lower HRQOL and perceived value of health scores ($\leq$25th percentile) and higher psychiatric symptom scores (SCL-90R GSI $\geq$63) after also adjusting for treatment group, age, education, and time-weighted HbA_{1c} level. Only the effect of LUTS in men on the EQ-5D score was nonsignificant. Similar results were found for the SF-36 for both men and women. No interactions between time-weighted HbA_{1c} and any urologic complication were found (Table 4).

We performed additional analyses for men with and without current problems with ED further divided into those with or without treatment for ED. We found that those with current complaints of ED, whether or not they were receiving treatment, had similar HRQOL scores that were consistently lower than men without complaints without regard to treatment (Supplementary Table 2). Finally, we used the full IIEF to analyze ED and found substantially the same results as those reported for the single ED

Table 1—Characteristics of participants by sex and treatment group at EDIC year 17

	EDIC year 17 (2010)			
	Men		Women	
Characteristic	INT (n = 320)	CONV (n = 324)	INT (n = 303)	CONV (n = 277)
Race (% white)	96.3	96.9	96.0	96.8
Age (years)	51.7 ± 6.7	51.5 ± 6.5	51.4 ± 7.2	49.8 ± 7.1†
College graduate (%)	62.7	65.7	57.8	59.9
Married (%)	72.6	75.2	69.8	70.1
Current cigarette smoker (%)	13.2	10.1	12.2	11.4
Current drinker (%)	52.7	50.0	36.3	43.2
BMI (kg/m^2)	29.0 ± 5.2	28.8 ± 4.3	29.2 ± 6.1	27.9 ± 5.6*
BMI category (%)				
Normal (BMI <25 kg/m^2)	23.4	18.6	25.6	30.3*
Overweight (BMI 25 to <30 kg/m^2)	42.1	43.3	37.4	42.9
Obese (BMI ≥30 kg/m^2)	34.5	38.1	37.0	26.8
Duration of diabetes (years)	30.0 ± 5.0	29.0 ± 4.6†	29.8 ± 5.0	29.9 ± 5.2
DCCT/EDIC time-weighted HbA_{1c} (%)	7.7 ± 1.0	8.2 ± 0.9†	7.8 ± 0.9	8.2 ± 0.9†
DCCT/EDIC time-weighted HbA_{1c} (mmol/mol)	61 ± 10	66 ± 10†	62 ± 10	67 ± 10†
DCCT cohort assignment (% primary prevention)	46.3	53.1	51.2	49.8
Retinopathy (%)‡	12.2	28.1†	10.2	24.2†
Nephropathy (%)§	4.7	9.6*	2.3	4.0
Neuropathy (%)‖	28.8	41.0†	21.2	26.0
DCCT/EDIC time-weighted blood pressure				
Systolic (mmHg)	120.8 ± 7.4	120.9 ± 7.5	116.6 ± 8.2	115.8 ± 8.6
Diastolic (mmHg)	76.1 ± 4.9	76.0 ± 4.5	72.7 ± 5.0	72.1 ± 4.9
Hypertension (%)¶	67.9	71.7	62.9	60.2
DCCT/EDIC time-weighted lipids				
Cholesterol (mg/dL)	179.9 ± 23.8	176.2 ± 25.1	185.5 ± 23.6	183.4 ± 23.2
LDL cholesterol (mg/dL)	110.8 ± 20.4	108.4 ± 21.7	108.9 ± 20.4	107.2 ± 20.3
ED	29.5	31.7	—	—
LUTS	23.5	25.6	22.8	21.4
FSD	—	—	28.9	23.6
UI	—	—	32.1	27.9

Data are means ± SDs or %. INT, intensive; CONV, conventional. *$P < 0.05$; †$P < 0.01$ for treatment group differences comparing INT vs. CONV by the Wilcoxon rank sum test for ordinal and numeric variables or the contingency χ^2 for categorical variables. ‡Retinopathy defined as PDR or worse up through EDIC year 14 using the Early Treatment Diabetic Retinopathy Study on a scale of 0–23 (≥12 PDR). §Nephropathy defined as any AER ≥300 mg/24 h or ESRD at EDIC year 15/16. ‖Neuropathy defined as confirmed clinical neuropathy at EDIC year 13/14. ¶Hypertension 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.

question about confidence in having an erection (data not presented).

CONCLUSIONS

Our findings show a negative effect of lower urinary tract complications and sexual dysfunction on measures of general and diabetes-specific HRQOL, perceived value of health, and psychiatric symptoms in men and women with longstanding type 1 diabetes. The magnitude of these effects was typically in the range of 5 points on both the SF-36 and DQOL scales, a difference considered clinically meaningful based on prior research (3,19,20). Moreover, using the clinical cutoff score for the SCL-90R GSI of ≥63, we found consistent effects of these complications on psychiatric symptoms. Such differences have also been found to be clinically relevant (25). These effects were seen after adjusting for key covariates, including treatment group, age, education level, and HbA_{1c} level. No interactions were found between time-weighted HbA_{1c} and any urologic complication. These effects were also found when history of diagnosis and treatment for depression was entered as a covariate in these models. Of interest, our analyses of ED, with and without treatment and current symptoms, underline the value of successful treatment of ED, in that those with ED who were successfully treated had almost identical HRQOL reports as those who never experienced ED.

Multivariable analyses, taking into account the presence of other serious diabetes complications (retinopathy, nephropathy, and neuropathy), further revealed that LUTS and sexual dysfunction had independent effects on HRQOL, perceived value of health, and psychiatric symptoms in both men and women. This underlines the effect of urologic conditions on patient perceptions of well-being even when other classic diabetes complications are evident. The presence of cardiovascular complications was not modeled in these analyses because the study group remained blinded to the findings from cardiovascular evaluations when these analyses were performed.

Table 2—Mean HRQOL scores of men and women by urologic complication status at EDIC year 17*

	ED		LUTS		FSD		LUTS	
HRQOL measure	ED	No ED	LUTS	No LUTS	FSD	No FSD	UI/LUTS	No UI/LUTS
Subjects, *n* (%)	194 (31)	440 (69)	158 (25)	485 (75)	146 (26)	408 (74)	233 (40)	343 (60)
Total DQOL score†	70.2 ± 0.8	78.3 ± 0.5	71.5 ± 0.9	77.1 ± 0.5	70.2 ± 0.9	74.6 ± 0.5	70.1 ± 0.7	75.4 ± 0.6
EQ-5D preference weighted mean‡	0.82 ± 0.01	0.90 ± 0.01	0.84 ± 0.01	0.89 ± 0.01	0.80 ± 0.01	0.87 ± 0.01	0.79 ± 0.01	0.89 ± 0.01
SF-36 subscales†								
Physical Function	78.7 ± 1.3	90.1 ± 0.9	80.8 ± 1.5	88.3 ± 0.9	75.4 ± 1.9	84.4 ± 1.1	75.1 ± 1.5	86.1 ± 1.2
Social Function	73.1 ± 1.2	80.8 ± 0.8	73.2 ± 1.4	80.1 ± 0.8	69.7 ± 1.7	75.3 ± 1.0	68.9 ± 1.3	77.3 ± 1.1
Role Function Physical	74.3 ± 2.2	87.0 ± 1.5	74.3 ± 2.5	85.8 ± 1.4	69.3 ± 3.1	78.6 ± 1.8	66.0 ± 2.4	82.0 ± 2.0
Role Function Emotional	79.6 ± 2.2	88.2 ± 1.5	76.9 ± 2.5	88.2 ± 1.4	76.6 ± 2.9	81.6 ± 1.7	73.4 ± 2.4	84.7 ± 1.9
Mental Health	72.4 ± 1.2	79.8 ± 0.8	71.6 ± 1.3	79.4 ± 0.7	69.5 ± 1.5	76.3 ± 0.9	71.5 ± 1.1	76.6 ± 1.0
Vitality	50.0 ± 1.5	62.8 ± 1.0	50.2 ± 1.7	61.7 ± 1.0	45.9 ± 1.9	55.5 ± 1.1	47.4 ± 1.5	55.9 ± 1.2
Bodily Pain	71.2 ± 1.3	77.7 ± 0.9	70.7 ± 1.5	77.2 ± 0.8	65.0 ± 1.8	73.5 ± 1.1	66.3 ± 1.4	74.6 ± 1.2
General Health Perception	51.9 ± 1.5	68.0 ± 1.0	55.7 ± 1.8	65.2 ± 1.0	55.3 ± 1.9	64.2 ± 1.1	56.6 ± 1.4	64.9 ± 1.2
SCL-90R T score§								
GSI	53.9 ± 0.8	47.7 ± 0.5	55.0 ± 0.9	47.9 ± 0.5	55.8 ± 1.0	51.3 ± 0.6	56.3 ± 0.8	50.0 ± 0.7
Depression	56.4 ± 1.0	47.0 ± 0.7	57.1 ± 1.2	47.6 ± 0.7	59.6 ± 1.4	51.7 ± 0.9	59.3 ± 1.1	50.2 ± 0.9

Data are least square means ± SEs adjusted for EDIC year 17 age and education. Sample sizes vary based on availability of HRQOL data. *All comparisons are significant at $P < 0.01$, with the exception of in women FSD vs. no FSD Role Function Physical ($P = 0.0105$) and Role Function Emotional (P = NS). †DQOL and SF-36 scores range from 0 to 100, where 100 indicates a more favorable quality of life. ‡The EQ-5D utility score ranges from 0 to 1, where 1 indicates a more favorable quality of life. §SCL-90R scores are converted to standard T scores by referring to the appropriate population-based norm tables. T scores have a mean of 50, SD of 10, and normal range from 40 to 60. A possible mental disorder is defined as a GSI T score ≥63.

Although directly comparing our results with those from patients with type 2 diabetes is not possible, these findings are consistent with population-based, community studies in type 2 diabetes. For example, the BACH study (7,30) examined the prevalence of urologic symptoms (including LUTS and urinary leakage) among 5,506 men and women and compared its effect on two SF-12 scales (Mental Health and Physical Function) with the effects of other self-reported medical conditions such as heart disease and diabetes. In BACH, the effect of LUTS and urine leakage on the SF-12 Physical Function scale was comparable to those of the other medical conditions, and the magnitude of the effects of these urologic symptoms on the SF-12 Mental Health scale was greater than of the other medical conditions (7,30). In a study of male patients with type 2 diabetes, with and without ED, who were older and had more comorbidities, SF-36 scale scores were typically lower than those of our subjects, but the differences between those with ED and without ED were of a similar magnitude (8). Our findings also expand on earlier preliminary evidence regarding HRQOL effects of urologic

Table 3—Adjusted odds of a low HRQOL score (≤25th percentile) by urologic complication status in men and women at EDIC year 17

	Urologic complications in men			Urologic complications in women		
	ED only (*n* = 115) vs.	LUTS only (*n* = 79) vs.	ED and LUTS (*n* = 79) vs.	FSD only (*n* = 71) vs.	UI/LUTS only (*n* = 147) vs.	FSD and UI/LUTS (*n* = 75) vs.
HRQOL measure	No ED or LUTS (*n* = 361)			No FSD or UI/LUTS (*n* = 259)		
Total DQOL score	3.2 (1.9–5.4)	2.6 (1.5–4.8)	7.2 (4.0–13.2)	3.0 (1.6–5.9)	3.1 (1.8–5.3)	4.6 (2.5–8.7)
EQ-5D preference weighted mean	1.9 (1.2–3.0)	0.9 (0.5–1.6)	4.0 (2.2–7.2)	2.8 (1.5–5.3)	3.4 (2.1–5.7)	5.3 (2.9–10.0)
SF-36 subscales						
Physical Function	2.9 (1.8–4.9)	2.0 (1.1–3.5)	7.7 (4.3–13.9)	2.1 (1.1–4.1)	2.4 (1.4–4.0)	3.7 (2.0–6.8)
Social Function	2.9 (1.8–4.7)	2.3 (1.4–4.0)	4.3 (2.4–7.4)	2.8 (1.6–5.0)	2.7 (1.7–4.2)	2.2 (1.3–4.0)
Role Function Physical	2.5 (1.5–4.1)	2.9 (1.6–5.1)	4.6 (2.6–8.2)	2.1 (1.1–4.0)	2.7 (1.6–4.4)	2.9 (1.6–5.4)
Role Function Emotional	2.1 (0.9–4.8)	2.5 (1.0–6.2)	2.3 (0.9–6.0)	2.1 (1.2–3.9)	2.4 (1.5–3.8)	1.8 (1.0–3.3)
Mental Health	3.1 (1.8–5.1)	2.2 (1.2–4.0)	4.0 (2.2–7.2)	3.1 (1.7–5.8)	2.6 (1.6–4.3)	2.1 (1.1–4.1)
Vitality	2.5 (1.5–4.1)	2.5 (1.4–4.4)	5.0 (2.8–8.9)	4.1 (2.2–7.4)	2.8 (1.8–4.6)	4.0 (2.2–7.2)
Bodily Pain	1.7 (1.1–2.7)	2.0 (1.2–3.3)	2.5 (1.5–4.3)	2.2 (1.3–3.9)	1.8 (1.2–2.7)	2.9 (1.6–5.1)
General Health Perception	4.0 (2.4–6.7)	2.1 (1.1–3.9)	6.5 (3.6–11.7)	3.9 (2.0–7.4)	2.5 (1.5–4.2)	3.5 (1.9–6.7)
SCL-90 GSI T score*	2.7 (1.2–6.0)	3.1 (1.3–7.4)	8.9 (3.9–20.0)	4.4 (2.0–10.1)	3.9 (1.9–7.8)	5.7 (2.5–12.6)

Each row represents one multivariate logistic regression model. Data are odds ratios (95% CI) adjusted for treatment group, EDIC year 17 age and education, and DCCT/EDIC time-weighted HbA_{1c}. Sample sizes vary based on availability of HRQOL data. *SCL-90 scores are converted to standard T scores (ranging from 30 to 80) by referring to the appropriate population-based norm tables. T-scores have a mean of 50, SD of 10, and normal range from 40 to 60. A possible mental disorder is defined as a GSI T score ≥63.

Table 4—Modeling the association among urologic complications, microvascular complications, and the presence of a low HRQOL score (≤25th percentile) in men and women at EDIC year 17

	Urologic complications in men		Microvascular complications		
HRQOL measure	ED (*n* = 194) vs. no ED (*n* = 440)	LUTS (*n* = 158) vs. no LUTS (*n* = 485)	Retinopathy*	Nephropathy†	Neuropathy‡
Total DQOL score	3.0 (1.9–4.7)	2.7 (1.7–4.2)	0.7 (0.4–1.2)	0.9 (0.4–2.0)	1.0 (0.6–1.6)
EQ5D preference weighted mean	2.1 (1.4–3.3)	1.3 (0.8–2.0)	0.8 (0.5–1.4)	1.1 (0.5–2.3)	1.6 (1.0–2.4)
SF-36 subscales					
Physical Function	2.7 (1.8–4.3)	1.9 (1.2–3.1)	0.9 (0.5–1.6)	2.0 (0.9–4.2)	2.1 (1.3–3.3)
Social Function	2.3 (1.5–3.5)	1.8 (1.2–2.8)	0.8 (0.5–1.3)	0.7 (0.3–1.5)	1.3 (0.8–1.9)
Role Function Physical	1.8 (1.1–2.8)	2.2 (1.4–3.4)	1.0 (0.6–1.8)	1.8 (0.9–3.8)	1.5 (0.9–2.3)
Role Function Emotional	1.8 (0.9–3.7)	1.8 (0.9–3.7)	0.9 (0.4–2.0)	0.5 (0.1–1.9)	1.4 (0.6–2.9)
Mental Health	2.3 (1.5–3.6)	1.8 (1.1–2.8)	1.0 (0.6–1.6)	0.7 (0.3–1.5)	1.4 (0.9–2.2)
Vitality	2.2 (1.4–3.4)	2.2 (1.4–3.5)	1.0 (0.6–1.7)	0.8 (0.4–1.8)	1.3 (0.8–2.1)
Bodily Pain	1.4 (0.9–2.1)	1.6 (1.1–2.5)	0.7 (0.4–1.1)	1.1 (0.6–2.3)	1.9 (1.2–2.8)
General Health Perception	3.3 (2.1–5.3)	1.8 (1.1–2.9)	1.0 (0.6–1.7)	1.3 (0.6–2.7)	1.4 (0.9–2.3)
SCL-90 GSI T score§	2.9 (1.5–5.7)	3.7 (1.9–7.2)	0.5 (0.2–1.2)	2.2 (0.8–6.0)	1.0 (0.5–2.0)
	Urologic complications in women		Microvascular complications		
	FSD (*N* = 146) vs. no FSD (*N* = 408)	UI/LUTS (*N* = 233) vs. no UI/LUTS (*N* = 343)	Retinopathy*	Nephropathy†	Neuropathy‡
Total DQOL score	2.0 (1.2–3.3)	2.7 (1.7–4.2)	2.0 (1.1–3.8)	0.6 (0.2–2.2)	1.1 (0.6–2.1)
EQ5D preference weighted mean	2.1 (1.3–3.4)	3.0 (2.0–4.7)	1.3 (0.7–2.5)	0.4 (0.1–1.7)	1.0 (0.5–1.7)
SF-36 subscales					
Physical Function	1.8 (1.1–2.9)	2.3 (1.5–3.6)	1.7 (0.9–3.3)	0.9 (0.2–3.3)	1.6 (0.9–2.9)
Social Function	1.6 (1.0–2.5)	1.9 (1.3–2.8)	1.3 (0.8–2.4)	0.9 (0.3–2.8)	0.8 (0.5–1.4)
Role Function Physical	1.6 (1.0–2.5)	2.2 (1.4–3.3)	1.0 (0.5–1.8)	0.8 (0.2–2.8)	1.5 (0.9–2.6)
Role Function Emotional	1.3 (0.8–2.0)	1.7 (1.1–2.5)	1.0 (0.5–1.8)	0.7 (0.2–2.6)	1.1 (0.6–1.9)
Mental Health	1.6 (1.0–2.6)	1.7 (1.1–2.6)	1.8 (1.0–3.3)	0.4 (0.1–1.8)	0.9 (0.5–1.7)
Vitality	2.4 (1.5–3.7)	2.1 (1.4–3.1)	1.1 (0.6–2.0)	1.2 (0.4–3.7)	1.3 (0.8–2.2)
Bodily Pain	2.1 (1.3–3.2)	1.7 (1.2–2.5)	0.9 (0.5–1.6)	0.4 (0.1–1.2)	1.6 (1.0–2.7)
General Health Perception	2.2 (1.4–3.6)	1.8 (1.2–2.9)	1.5 (0.8–2.7)	3.1 (0.9–10.8)	1.8 (1.1–3.1)
SCL-90 GSI T score§	2.7 (1.5–4.8)	2.3 (1.3–4.0)	1.4 (0.6–2.9)	—	0.9 (0.5–1.9)

Each row represents one multivariate logistic regression model. Data are odds ratios (95% CI) adjusted for treatment group, EDIC year 17 age and education, and DCCT/EDIC time-weighted HbA_{1c}. Sample sizes vary based on availability of HRQOL data. *Retinopathy defined as PDR or worse up through EDIC year 14 using the Early Treatment Diabetic Retinopathy Study on a scale of 0–23 (≥12 PDR). †Nephropathy defined as any AER ≥300 mg/24 h or ESRD at EDIC year 15/16. ‡Neuropathy defined as confirmed clinical neuropathy at EDIC year 13/14. §SCL-90 scores are converted to standard T scores (ranging from 30 to 80) by referring to the appropriate population-based norm tables. T scores have a mean of 50, SD of 10, and normal range from 40 to 60. A possible mental disorder is defined as a GSI T score ≥63. There were no subjects with a GSI T score ≥63 and nephropathy.

symptom reports in the EDIC study (3). Finally, prior research (8,24) and our findings indicate a substantial effect on psychiatric symptoms overall and depressive symptoms in particular. This study further suggests that the relationship of urologic complications with psychiatric symptoms was not due to the presence of an underlying affective disorder.

Our study has unique strengths, including a large sample size of patients with type 1 diabetes; detailed demographic and biomedical information collected using standardized methods; a comprehensive set of well-validated indicators of HRQOL, perceived value of health, and psychiatric symptoms; careful assessment of multiple urologic complications and symptoms; and a wide range of clinical outcomes.

The study also has limitations. Assessment of urologic complications depends on patient self-report. There may be inherent biases, such as some patients with more serious HRQOL problems reporting more urologic complications, thereby exaggerating the relationship. The role of medications used in the treatment of comorbidities, such as hypertension and urologic symptoms, particularly ED, is difficult to ascertain because EDIC is a natural history study with wide variation in the type and timing of medication use. Medications may directly or indirectly affect HRQOL and psychiatric symptom reports. Furthermore, although the DCCT/EDIC participants have been followed up longitudinally, this study is based on cross-sectional assessments of HRQOL and urologic complications and current status of other diabetes complications. Therefore, direction of causality cannot be determined.

Other limitations can affect the generalizability of its findings. The subjects were long-term participants in a clinical trial and follow-up study and therefore are likely to be different from the general population. They have a relatively high average socioeconomic status and education level and are predominantly Caucasian. Such selection biases could affect the findings because typical patients would likely have more serious complications.

With improved treatment, patients with type 1 diabetes are experiencing slower progression of life-threatening complications; therefore, chronic morbidities, such as urologic complications,

may become more important sources of reduced HRQOL. This study and others underline the magnitude urologic problems in populations with and without diabetes and the effect that these problems have on patients' personal lives (7,8,31).

Because urologic symptoms and, in particular, sexual dysfunction can be an embarrassing and therefore a difficult topic for patients to discuss in clinical practice, information from this study can provide useful guidance for practitioners caring for patients with diabetes. Specific inquiries and use of self-report measures may help gather information about such sensitive topics in order to engage in discussions of therapies that can address urologic symptoms.

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