## UCSF UC San Francisco Previously Published Works

## Title

Sexual dysfunction in women with type 1 diabetes: long-term findings from the DCCT/ EDIC study cohort.

**Permalink** https://escholarship.org/uc/item/0568r0n2

**Journal** Diabetes care, 32(5)

**ISSN** 0149-5992

## Authors

Enzlin, Paul Rosen, Raymond Wiegel, Markus <u>et al.</u>

Publication Date 2009-05-01

## DOI

10.2337/dc08-1164

Peer reviewed

# Sexual Dysfunction in Women With Type 1 Diabetes

Long-term findings from the DCCT/ EDIC study cohort

PAUL ENZLIN, PHD<sup>1,2</sup> RAYMOND ROSEN, PHD<sup>3,4</sup> MARKUS WIEGEL, PHD<sup>3,4</sup> JEANETTE BROWN, MD<sup>5</sup> HUNTER WESSELLS, MD<sup>6</sup>

PATRICIA GATCOMB, RN, CDE<sup>7</sup> BRANDY RUTLEDGE, PHD<sup>8</sup> KA-LING CHAN, MS<sup>8</sup> PATRICIA A. CLEARY, MS<sup>8</sup> THE DCCT/EDIC RESEARCH GROUP\*

**OBJECTIVE** — This study aimed to investigate the prevalence and risk factors associated with sexual dysfunction in a well-characterized cohort of women with type 1 diabetes.

**RESEARCH DESIGN AND METHODS** — The study was conducted in women enrolled in the long-term Epidemiology of Diabetes Interventions and Complications (EDIC) study, a North American study of men and women with type 1 diabetes. At year 10 of the EDIC study, 652 female participants were invited to complete a validated self-report measure of sexual function, standardized history and physical examinations, laboratory testing, and mood assessment.

**RESULTS** — Of the sexually active women with type 1 diabetes in the EDIC study, 35% met criteria for female sexual dysfunction (FSD). Women with FSD reported loss of libido (57%); problems with orgasm (51%), lubrication (47%), and arousal (38%); and pain (21%). Univariate analyses revealed a positive association between FSD and age (P = 0.0041), marital status (P = 0.0016), menopausal status (P = 0.0019), microvasculopathy (P = 0.0092), and depression (P = 0.0022). However, in a multivariate analysis, only depression (P = 0.004) and marital status (P = 0.003) were significant predictors of FSD.

**CONCLUSIONS** — FSD is common in women with type 1 diabetes and affects all aspects of sexual function and satisfaction. Depression is the major predictor of sexual dysfunction in women with type 1 diabetes. These findings suggest that women with type 1 diabetes should be routinely queried about the presence of sexual dysfunction and possible co-association with depression.

#### Diabetes Care 32:780-785, 2009

iabetes has long been considered a major cause of impaired sexual function. Both men with type 1 and type 2 diabetes have been shown to have substantially increased risk of erectile dysfunction (ED) (1–5). Beyond the effects of comorbidities, such as older age, use of antihypertensive medication, high BMI, and smoking, the severity and duration of diabetes and its vascular and neurological complications, which cause abnormalities in the endothelium or nitric

From the <sup>1</sup>Department of Psychiatry, Katholieke Universiteit Leuven & University Hospitals Gasthuisberg, Leuven, Belgium; the <sup>2</sup>Department of Obstetrics and Gynaecology, Institute for Family and Sexuality Studies, Katholieke Universiteit Leuven & University Hospitals Gasthuisberg, Leuven, Belgium; the <sup>3</sup>New England Research Institutes, Watertown, Massachusetts; the <sup>4</sup>Robert Wood Johnson Medical School, University of Medicine & Dentistry, Piscataway, New Jersey; the <sup>5</sup>Department of Obstetrics, Gynecology and Reproductive Sciences, University of California San Francisco Women's Health Clinical Research Center, San Francisco, California; the <sup>6</sup>Department of Urology, University of Washington, Seattle, Washington; <sup>7</sup>Yale University School of Medicine, New Haven, Connecticut; and <sup>8</sup>The Biostatistics Center, The George Washington University, Rockville, Maryland.

Corresponding author: Paul Enzlin, paul.enzlin@uz.kuleuven.ac.be.

Received 15 August 2008 and accepted 2 February 2009.

\*A complete list of participants in the DCCT/EDIC Research Group can be found in Arch Ophthalmol 2008;126:1707–1715.

DOI: 10.2337/dc08-1164

© 2009 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. See http://creativecommons. org/licenses/by-nc-nd/3.0/ for details.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

oxide–related mechanisms in the corpora cavernosa, have been strongly linked with the development of sexual dysfunction in men (1,4,5).

Women with diabetes have similar rates of cardiovascular and neurological complications, and therefore similar rates of sexual dysfunction might be anticipated. Sexual functioning of women with diabetes, however, has received far less attention in research, and results are less conclusive than those of studies in men (6). In general, studies of sexual dysfunction in women have lagged behind those in men, likely due to several factors, including a lack of standardized definitions of sexual dysfunction in women, absence of well-validated scales, and societal taboos regarding female sexuality (7,8). Previous studies of sexual dysfunction in women with diabetes are small in number and have significant methodological drawbacks, including small sample sizes and lack of adequate characterization of diabetes, particularly with regard to glycemic control, neurovascular complications, psychological adjustment to diabetes, and presence or absence of comorbid depression (6).

Nevertheless, preliminary reports have noted a high prevalence of sexual dysfunction in women with diabetes. In particular, a mixed pattern of sexual symptoms has been found, including loss of sexual interest or desire, arousal or lubrication difficulties, painful intercourse (dyspareunia), and loss of the ability to reach orgasm (6). In a recent study, women with type 1 diabetes had increased rates of sexual dysfunction compared with age-matched control subjects (9). In contrast to studies in men, no association was found between sexual dysfunction and cardiovascular, metabolic (i.e., glycemic control, diabetes duration), or other risk factors (i.e., age, BMI, menopause, use of hormone replacement therapy) (9). Another study further revealed that sexual dysfunction in women with diabetes is related more directly to psychological factors, i.e., the presence of depression was found to be the major predictor of female sexual dysfunction

(FSD) (10). This latter finding is consistent with other studies showing depression to be a major risk and comorbid factor of FSD (3).

To summarize, there are few data available that have systematically evaluated the effect of diabetes and/or the role of specific diabetes therapies on female sexual functioning. The Diabetes Control and Complications Trial (DCCT)/ Epidemiology of Diabetes Interventions and Complications (EDIC) study is unique in providing the opportunity to assess female sexual function in the context of a large, multicenter, controlled trial of long-term therapy for type 1 diabetes. Accordingly, this study aimed to evaluate the prevalence, type, risk factors, and predictors of FSD in a prospective observational study examining the risk factors associated with long-term complications of type 1 diabetes in women (11).

#### **RESEARCH DESIGN AND**

**METHODS** — The original cohort of the DCCT consisted of 1,441 men and women 13–39 years of age at study entry. The primary prevention cohort consisted of 726 subjects with no retinopathy, a urinary albumin excretion rate <40 mg/24 h, and a diabetes duration of 1-5 years. The secondary intervention cohort consisted of 715 subjects who had nonproliferative retinopathy, urinary albumin excretion rate ≤200 mg/24 h, and a diabetes duration of 1-15 years (11). They entered the DCCT trial between 1983 and 1989 and were studied for an average of 6.5 years. In total, 730 patients were randomly assigned to receive conventional diabetes treatment, and 711 were randomized to receive intensive diabetes treatment. In 1993, the DCCT was discontinued due to statistical evidence of a powerful salutary effect of intensive treatment on long-term complications (12). At study close-out, DCCT subjects were encouraged to use intensive therapy and invited to join the EDIC study, a multicenter longitudinal observational study. Of the 1,428 surviving members of the original cohort, 1,375 (95%) elected to participate in some or all aspects of the EDIC study (13). At EDIC year 10, 1,365 patients (713 men and 652 women) were invited to complete self-report measures of sexual dysfunction and urological complications (i.e., bladder dysfunction and urinary tract infections). A total of 550 (84.4%) of the 652 women completed the Uro-EDIC questionnaire.

On the annual anniversary of enrolling in the DCCT, each EDIC subject underwent a standardized annual history and physical examination, including a detailed evaluation of overall health, diabetes management, occurrence of diabetes complications, development of new disease, and medications used. Annual evaluations also include resting electrocardiograms, Doppler ultrasound measurements of ankle and arm blood pressure ratios, and arm blood pressure. Serum creatinine and A1C are assessed annually using the same methods as in the DCCT (12,13,14). Lipid profiles and 4-h urine collections for measurement of albumin excretion rate and creatinine clearance are obtained on alternate years using the same methods as in the DCCT (13). Hypertension was defined as systolic blood pressure  $\geq 140$ mmHg, diastolic blood pressure  $\geq 90$ mmHg, or documented use of antihypertensive agents. Hypercholesterolemia was defined as LDL cholesterol ≥130 mg/dl or use of lipid-lowering agents.

Sexual function was evaluated by an abbreviated version of the Female Sexual Function Index (FSFI) (15). The FSFI is a widely used, multidimensional, wellvalidated, self-report measure that assesses sexual function across six domains, including sexual desire, arousal, lubrication, orgasm, satisfaction, and pain (15,16,17,18). For the present study, an abbreviated version including 7 of the 19 original FSFI items was developed (FSFI-R). From each of the domains of sexual desire, arousal, lubrication, orgasm, and pain, one item was included together with two items from the sexual satisfaction domain. The items are 5-point Likert-type items, with higher scores reflecting worse sexual functioning. The FSFI-R total score is the sum of all the items representing each domain of sexual functioning added with the mean score of the two items assessing satisfaction. The psychometric properties of the FSFI-R were evaluated using an independent sample of 286 women with and 245 women without sexual dysfunction selected from previous validation studies (16,17,18). Overall, the abbreviated version of the FSFI was found to have adequate psychometric properties that are essentially equivalent to those of the full-scale measure (see the online appendix available at http:// care.diabetesjournals.org/cgi/content/full/ dc08-1164/DC1).

The prevalence of a specific sexual problem was estimated based on a domain-specific item analysis by combining the percentages of women who scored in the two lowest categories on each item ["Almost never or never" or "A few times (less than half the time)"], except for the pain domain where the percentages of women who scored in the highest categories on each item ["Almost always or always" or "Most times (more than half the time)"] were combined. For example, the prevalence of dyspareunia (painful intercourse) was based on the percentage of women who answered "most times (more than half the time)" or "almost always or always" to the question "How often did you experience discomfort or pain during vaginal penetration?"

In this study, the prevalence of depression was assessed by means of a composite depression variable, which was based on study coordinator ratings of clinical depression, based on DSM-IV criteria, in addition to patient self-reports of use of antidepressant medications and/or psychological counseling for depressive symptoms.

#### Data analysis

Initially, Pearson's  $\chi^2$  tests (Fisher's exact where appropriate) were used to assess univariate associations between sexual function scores (both total and individual domain scores) and relevant biomedical and psychosocial predictor variables. For continuous measures, a nonparametric Kruskal-Wallis test was used. Those variables that were nominally significant at the P < 0.15 level, with respect to overall FSD, with no adjustment for multiple comparisons, were used in a multivariate logistic regression model. An identical analysis was performed using the same covariates for each of the individual sexual domains, where "FSD" is a score  $\leq 2$ and "no FSD" is a score >2 for each domain item, except for the pain domain, where the opposite was true. FSD in the satisfaction domain was indicated by a total mean score  $\leq 2$ . Due to the model selection and the multiple testing, only effects nominally significant at  $P \leq 0.01$ are cited. Analyses were performed using SAS version 8.2 (SAS Institute, Cary, NC).

**RESULTS** — The design, methods, baseline findings, and main outcomes of the DCCT and EDIC study (to date) have been published elsewhere (11,12). A total of 550 women completed the Uro-EDIC questionnaire (response rate 84.4%). This cohort had lower triglyceride levels (P = 0.0389), had lower A1C levels (P = 0.0029), and smoked less (P = 0.0060) at

#### Table 1—*Clinical characteristics of the female Uro-EDIC cohort* (N = 424)

	DCCT baseline (1983–1989)		9)	Year 10 EDIC (2003)		
	Conventional	Intensive	Р	Conventional	Intensive	Р
n	217	207		217	207	
Sociodemographic						
Age (years)	$24.9 \pm 7.2$	$26.4 \pm 7.2$	0.03	$42.0 \pm 7.0$	$43.6 \pm 7.1$	0.02
Race*	209 (96.3)	200 (96.6)		209 (96.3)	200 (96.6)	
White, not of Hispanic origin	5 (2.3)	3 (1.4)	0.09*	5 (2.3)	3 (1.4)	0.09*
Black, not of Hispanic origin	0 (0.0)	4 (1.9)		0 (0.0)	4 (1.9)	
Hispanic	2 (0.9)	0 (0.0)		2 (0.9)	0 (0.0)	
Asian or Pacific Islander	1 (0.5)	0 (0.0)		1 (0.5)	0 (0.0)	
Married	94 (43.3)	98 (47.3)	0.41	167 (78.4)	168 (83.2)	0.22
Cigarette smoker†	30 (13.8)	33 (15.9)	0.54	27 (12.7)	32 (15.8)	0.37
Diabetes treatment and control						
Cohort						
Primary	101 (46.5)	104 (50.2)	0.45	_	_	0.45
Secondary	116 (53.5)	103 (49.8)		_	_	
Diabetes duration (years)	$6.0 \pm 4.3$	$5.9 \pm 4.3$	0.90	$22.8 \pm 5.1$	$22.8 \pm 5.0$	0.84
A1C (%)	$9.1 \pm 1.6$	$9.1 \pm 1.5$	0.85	$7.8 \pm 1.2$	$7.9 \pm 1.4$	0.67
Insulin dose (units $\cdot$ kg <sup>-1</sup> $\cdot$ day <sup>-1</sup> )	$0.70 \pm 0.27$	$0.69 \pm 0.25$	0.73	$0.61 \pm 0.24$	$0.61 \pm 0.21$	0.69
Microvascular complications						
Retinopathy‡						
Nonproliferative or none	217 (100.0)	207 (100.0)	0.66	123 (56.7)	165 (79.7)	< 0.001
Proliferative	0 (0.0)	0 (0.0)		94 (43.3)	42 (20.3)	
Nephropathy						
None (AER $<$ 40 mg/24 h)	209 (96.3)	195 (94.2)	0.31	153 (70.5)	174 (84.1)	0.002
Microalbuminuria (AER 40–299 mg/24 h)	8 (3.7)	12 (5.8)		49 (22.6)	29 (14.0)	
Albuminuria (AER ≥300 mg/24 h)	0 (0.0)	0 (0.0)		15 (6.9)	4 (1.9)	
Hypertension§	0 (0.0)	0 (0.0)	_	61 (28.6)	57 (28.1)	0.90
Creatinine clearance ml/min per $1.73 \text{ m}^2$	$124.8 \pm 30.0$	$123.7 \pm 27.9$	0.86	$110.0 \pm 28.0$	$110.8 \pm 28.0$	0.66
Peripheral neuropathy	7 (3.2)	7 (3.4)	0.93	156 (71.9)	121 (58.5)	0.004

Data are means  $\pm$  SD or *n* (%). \*Race as classified by the participant during the DCCT enrollment interview. †Defined as having ever smoked. ‡Determined by ETDRS (Early Treatment Diabetic Retinopathy Study) score on a scale of 0–23: <12 = nonproliferative,  $\geq$ 12 = proliferative. §Hypertension defined as sitting systolic blood pressure  $\geq$ 140 mmHg, diastolic blood pressure  $\geq$ 90 mmHg, or use of antihypertensive medication. ||Defined in the DCCT by the presence of definite clinically evident distal symmetrical polyneuropathy and an abnormal nerve conduction study or in the EDIC by the MNSI (Michigan neuropathy screening instrument): >6 positive responses on the questionnaire or a score >2 on the examination.

DCCT baseline compared with the total cohort of women who originally entered the DCCT. In addition, the sample who completed the survey did not differ on DCCT variables at baseline compared with the 102 women who did not participate in the study.

In total, 116 women (21.0%) were excluded from the analyses because they did not provide complete data on sexual functioning (n = 10) or reported lack of sexual activity (n = 52) or absence of a sexual partner (n = 54) during the previous 12 months. At the time of the survey, these 116 sexually inactive women differed from the 434 sexually active women in that they were less likely to be married or in a partner relationship (P < 0.0001), were more often randomized to intensive treatment (P = 0.0376), had a higher mean age (P = 0.0004), were more likely to be (post)menopausal (P = 0.0415), had a higher BMI (P = 0.0271), and had

an increased prevalence of hypertension (P = 0.0011). This report thus describes results obtained from 424 eligible participants: 217 in the conventional and 207 in the intensive treatment groups.

The mean age of the 424 participating women was  $42.8 \pm 7.1$  years with a mean duration of type 1 diabetes of  $22.8 \pm 5.0$ years. The majority of participants were Caucasian (97%), were married (81%), and had normal albumin excretion rates (77%). Table 1 presents socioeconomic and diabetic characteristics at DCCT baseline and at the year 10 Uro-EDIC examination by DCCT treatment group. At DCCT baseline, age was the only significant difference between treatment groups; the intensive group was slightly older (P = 0.03). However, at the year 10 examination in the EDIC study, women randomized to intensive treatment were less likely to have retinopathy, nephropathy, and peripheral neuropathy than

those randomized to conventional treatment.

# Prevalence and characteristics of sexual dysfunction

Based on the FSFI-R cutoff score for sexual dysfunction of 22.75, the overall prevalence of FSD among sexually active women in this study was found to be 35.4%. Univariate analyses revealed that women meeting criteria for FSD were on average older than women without FSD (P = 0.0041), were more likely to be married (P = 0.0016), be (post)menopausal (P = 0.0019), have evidence of microvasculopathy (composite diabetes complications variable, P = 0.0092), and be depressed (P = 0.0022) than women without FSD (Table 2). Among those women who met the criteria for FSD, 57% reported a problem with decreased desire, 51% had problems with orgasm, 47% had inadequate lubrication, 38%

Table 2—Clinical characteristics of UroEDIC women according to FSD status at year 10 of the
EDIC $(N = 424)^*$

	No ECD	FSD	Р
	No FSD	гзи	P
n	274	150	
Treatment group			0.8759
Conventional	141 (51.5)	76 (50.7)	
Intensive	133 (48.5)	74 (49.3)	
Cohort			0.4798
Primary	129 (47.1)	76 (50.7)	
Secondary	145 (52.9)	74 (49.3)	
Age (years)	$42.0 \pm 7.1$	$44.2 \pm 6.8$	0.0041
Race			0.4725
Non-Caucasian	11 (4.0)	4 (2.7)	
Caucasian	263 (96.0)	146 (97.3)	
Diabetes duration (years)	$22.7 \pm 5.0$	$23.0 \pm 5.1$	0.4688
Married (Yes )	205 (76.2)	130 (89.0)	0.0016
Hysterectomy (Yes)†	28 (10.2)	21 (14.0)	0.2443
Menopausal (Yes)‡	43 (16.2)	42 (29.2)	0.0019
Retinopathy§			
Nonproliferative or less	184 (67.2)	104 (69.3)	0.6456
Proliferative or greater	90 (32.8)	46 (30.7)	
Nephropathy (AER)			0.8178
Normal (AER <40 mg/24 h)	212 (77.4)	115 (76.7)	
Microalbuminuria (40–299 mg/24 h)	51 (18.6)	27 (18.0)	
Albuminuria (AER ≥300 mg/24 h)	11 (4.0)	8 (5.3)	
Peripheral neuropathy during the DCCT and	171 (62.4)	106 (70.7)	0.0876
EDIC (Yes)			
Composite complications variable¶			0.0092#
None	209 (76.3)	92 (61.3)	
One	51 (18.6)	45 (30.0)	
Two	9 (3.3)	9 (6.0)	
Three	5 (1.8)	3 (2.0)	
Four	0 (0.0)	1 (0.7)	
Depression (Yes)**	50 (18.2)	47 (31.3)	0.0022
A1C at DCCT eligibility (%)	$9.3 \pm 1.7$	$8.8 \pm 1.4$	0.0353
A1C at EDIC year 10 (%)	$7.9 \pm 1.3$	$7.8 \pm 1.2$	0.6031
DCCT mean A1C (%)	$8.2 \pm 1.4$	$8.1 \pm 1.5$	0.3464
Time-weighted DCCT/EDIC mean A1C	$8.1 \pm 1.0$	$8.0 \pm 1.1$	0.4061
BMI (kg/m <sup>2</sup> )	$27.0 \pm 5.0$	$27.6 \pm 4.8$	0.1912
Hypertension (Yes)††	75 (27.8)	43 (29.5)	0.7177
Medication usage			0.1.2.1
Antihypertensives at year 10‡‡	87 (33.6)	53 (36.8)	0.5160
Antidepressants at year 10§§	49 (17.9)	46 (30.7)	0.0025
	12 (11.2)	10 (50.1)	0.0025

Data are means  $\pm$  SD and *n* (%). Percentages are based on total sample size minus the number of missing values. \*Ten subjects did not answer the FSD question. †Hysterectomy defined as a subject's menstrual period ceasing and it being considered permanent due to surgery. #Menopause defined as a subject's menstrual period ceasing and it being considered permanent. §Determined by ETDRS (Early Treatment Diabetic Retinopathy Study) score on a scale of 0-23: <12 = nonproliferative,  $\geq 12 =$  proliferative. Defined in the DCCT by the presence of definite clinically evident distal symmetrical polyneuropathy and an abnormal nerve conduction study or in the EDIC by the MNSI (Michigan neuropathy screening instrument): >6 positive responses on the questionnaire or a score >2on the examination. [Variable has a score between (0 and 4) depending on the total number of "yes" responses to the question of ever having the following four complications: retinopathy (defined as scatter laser in both eyes), nephropathy (defined as AER >300 mg/24 h, serum creatinine >2 mg/dl, and standard clearance <60 ml/min per 1.73m<sup>2</sup> or dialysis and/or kidney transplant or defined by the MNSI: >6 positive responses on the questionnaire and a score  $\geq 2$  on the examination), and cardiovascular disease (defined as having any of the following six cardiovascular events: cardiovascular death, acute myocardial infarction, silent myocardial infarction, revascularization, confirmed angina, or cerebrovascular accident). #Fisher's exact test. \*\*Depression ascertained by the study coordinator on an annual review of psychiatric events that occurred in the year(s) since the last evaluation; if patient indicated "yes," then the coordinator completed a documentation form to get more information (e.g., where treated, if medication was prescribed, DSM-III diagnosis). Additionally, if the patients indicated that they regularly took antidepressants for depression and/or followed psychological counseling for depressive symptoms, they were included in the depression category.  $\dagger$ †Hypertension defined as sitting systolic blood pressure  $\geq$ 140 mmHg, diastolic blood pressure ≥90 mmHg, or use of antihypertensive medication. ‡‡Antihypertensive medication for any reason including use of ACE inhibitors and angiotensin II receptor blockers. §§Antidepressants defined by patient indicating regular usage of antidepressants on medication form.

had problems with sexual arousal, and 21% reported pain during intercourse. Additionally, 25% of sexually active women reported low overall sexual satisfaction. For all sexual domains, study participants without FSD scored higher (i.e., had better function) than women with FSD (P < 0.001).

#### FSD clinical predictors model

Univariate analyses were conducted to examine which variables predicted the presence or absence of sexual dysfunction in women with type 1 diabetes (Table 2). Those variables that were nominally significant at the P < 0.15 level, with respect to FSD, with no adjustment for multiple comparisons, were selected for further testing in a multivariate model. The outcome variable of "overall FSD" (based on a cutoff score of  $\geq 22.75$  on the FSFI-R) was regressed against the following predictor variables: treatment group (intensive/conventional), cohort (primary/ secondary), age (adolescent vs. adult), menopausal status, marital status, a composite variable of diabetes complications, peripheral neuropathy, clinical depression, and the log of the A1C at DCCT eligibility. When controlling for the effects of other variables, depression status (depressed vs. nondepressed) and marital status (married vs. not married) were the only variables in the multivariate model that were significant predictors of FSD. Women with type 1 diabetes in our sample who showed signs of depression were 2.08 times more likely to have FSD than women who were not depressed (adjusted odds ratio [OR] 2.08 [95% Wald CI 1.27-3.42]). Married women with type 1 diabetes were 2.49 times more likely to have FSD than women who were not married (2.49 [1.34-4.65]).

#### Individual sexual domain analysis

In addition to the relationship with each of the major predictor variables, the differences between the treatment groups in specific domains of sexual function were both univariately and multivariately analyzed. In the univariate analyses, associations were found between menopausal status, marital status, the composite diabetes complications variable, the log of A1C at DCCT baseline, and depression and the individual sexual domains. The multivariate results per individual sexual domain are summarized. Depression was a statistically significant risk factor for FSD in the arousal (OR for depressed vs. not depressed 2.47 [95% CI 1.31-4.66],

#### Sexual dysfunction in women with type 1 diabetes

P = 0.0062) and lubrication domains  $(2.41 \ [1.33-4.37], P = 0.0041)$ . The complex composite variable was statistically significant with respect to FSD in the lubrication (for three vs. none 2.82 [0.42-18.97], two vs. none 5.332 [1.61-17.65], and one vs. none 4.17 [2.19-[7.95], P < 0.0001) and orgasm domains (for three vs. none 3.20 [0.55–18.71], two vs. none 3.80 [1.19–12.18], and one vs. none 2.97 [1.62–5.45], P = 0.0021). Being married was the only significant risk factor for FSD in the desire domain (for married vs. not married 2.97 [1.48-5.93], P = 0.0008). Menopause was an important risk factor for FSD in the lubrication domain (for menopausal vs. not menopausal 2.45 [1.34-4.50], P = 0.0041).

**CONCLUSIONS** — This study aimed to investigate the prevalence and risk factors associated with FSD in a large wellcharacterized prospective cohort sample of women with type 1 diabetes (Uro-EDIC) using a validated measure of sexual function (FSFI-R). These findings are based on the largest well-characterized prospective cohort of women with type 1 diabetes in which sexual function has been evaluated. Considering the relatively young age (mean 43 years) of the study cohort, a prevalence rate of 35% for FSD can be regarded as moderately high. Given the decision not to include sexually inactive women in the analyses, this prevalence rate of 35% is rather a conservative estimate. The FSD prevalence rate in our study is slightly higher than those reported in previous studies of women with type 1 diabetes, which ranged from 27 to 29% (12,19). The fact that in previous studies different questionnaires were used and that participating women were even younger in age might (partially) account for the differences observed.

Although rates of sexual dysfunction in women are not dissimilar to those in men, the pattern of specific effects of diabetes on men and women is markedly different. While ED affects men both with type 1 and with type 2 diabetes, the most prevalent sexual dysfunction, lubrication and sexual arousal difficulties, were not the sole or the most prevalent problem in women. Moreover, ED is strongly correlated with A1C and the cardiovascular and neuropathic complications of diabetes (3,4,10). Again, in contrast, our study reveals in a multivariate analysis that FSD in women with type 1 diabetes is most strongly and consistently correlated with

depression and marital status. The lack of association between any measurement of A1C and FSD in this study suggests that compared with men, the sexual response in women with diabetes is more likely to be affected by the psychosocial aspects (e.g., depression) than by the metabolic control or complications of the disease. Similar results regarding the association between depression and FSD were observed in a previous study of younger women with type 1 diabetes (10). This finding is also consistent with results of other studies of sexually dysfunctional women, in which associations have been observed between FSD and depression (20). The current study thus provides further evidence for the hypothesis that in diabetic women, sexual dysfunction is more strongly related to psychosocial aspects rather than the typical pattern of cardiovascular- and metabolic-related risk factors observed in studies of men with diabetes (3,4,10).

Several explanations can be offered to account for the different pattern of effects in men and women. It is conceivable, for example, that these differences in sex risk factor profiles are due to differences in the underlying physiological mechanisms (e.g., differences in neurotransmitter involvement) of sexual response in men and women (21,22). As early as 1983, Schreiner-Engle (23) hypothesized that diabetes-related vasculopathy or neuropathy might be less readily perceived by women and that women with diabetes might not be aware of a relative decreased lubrication response and therefore not likely to report it, in contrast to men who readily experience and report ED. Alternatively, it has been proposed that, in general, cultural and/or psychosocial factors may play a larger role in female sexuality and that depression is a more prevalent and potentially more impactful factor in women (7). Because of the multidimensional etiology of FSD in women with diabetes, it will be necessary for future research to use a more comprehensive assessment of sexual function, including a combination of both subjective (i.e., standardized questionnaires) and objective methodology (i.e., vaginal plethysmography). In this respect, we should note that Wincze et al. (24), using vaginal plethysmography as an objective measure of physiological arousal, did find an association between diabetes and decreased vaginal lubrication in women. Further studies in this area would be valuable to test alternative hypotheses and to determine whether treating a mood disorder in women with type 1 diabetes contributes to improved sexual function independent of glycemic control.

Finally, some limitations of the study need to be acknowledged. Although this study is based on a prospective, longitudinal, observational study of treatment effects in patients with type 1 diabetes, the analyses presented are from a cross-sectional analysis of data obtained at 10-year follow-up. Future studies in this field should, therefore, use a true longitudinal design to more directly test sequence effects and order of changes in sexual function and to further elucidate the differences observed between the sexes. Also, since the population of the EDIC-study is in certain respects limited in its diversity (age, race, and diabetes type), the results of this study only apply to Caucasian, relatively young women with type 1 diabetes. Future research should attempt to include more diverse samples in order to examine the risk and risk factor of FSD in other groups. Third, we should reemphasize that the exclusion of sexually inactive women from our analyses most likely biases our overall prevalence findings (35%) in a conservative direction. However, by restricting our analyses to this group of women, we are able to ascertain specific effects on each of the sexual function domains in relation to specific risk factors or predictors. A final limitation is that no nondiabetic control women were included in the study, and we therefore relied on norms from previous clinical studies to interpret the prevalence of the sexual dysfunctions observed. However, this is not a serious limitation in view of the large body of published data on sexual dysfunction in the general population in both men and women.

In conclusion, the results of this study provide further evidence that women with type 1 diabetes are at risk for several sexual dysfunctions. In contrast to findings in men, our results showed that in women with type 1 diabetes, depression and marital status are the main predictors of FSD, whereas glycemic control and complications were not associated with FSD. Further studies are needed to elucidate the mechanisms underlying these differences. Considering that FSD can have an important negative effect on quality of life and partner relationships, the sexual difficulties of women with diabetes warrant more attention in both research

and practice. Similar to the annual evaluation of diabetes complications, women with type 1 diabetes should also be regularly queried about the presence of depressive symptoms, sexual function, and sexual satisfaction.

Acknowledgments— The DCCT/EDIC project is supported by contracts with the Division of Diabetes, Endocrinology, and Metabolic Diseases of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); National Eye Institute; National Institute of Neurological Disorders and Stroke; the General Clinical Research Centers Program and the Clinical and Translation Science Centers Program; and National Center for Research Resources and by Genentech through a Cooperative Research and Development Agreement with the NIDDK.

Contributors of free or discounted supplies and/or equipment: LifeScan, Roche, Aventis, Eli Lilly, OmniPod, Can-Am, BD, Animas, Medtronic, Medtronic MiniMed, Bayer, and OMRON.

No other potential conflicts of interest relevant to this article were reported.

#### References

- Brown JS, Wessells H, Chancellor MB, Howards SS, Stamm WE, Stapleton AE, Steers WD, Van Den Eeden SK, McVary KT. Urologic complications of diabetes. Diabetes Care 2005;28:177–185
- Rosen RC, Wing R, Schneider S, Gendrano N 3rd. Epidemiology of erectile dysfunction: the role of medical comorbidities and lifestyle factors. Urol Clin North Am 2005; 32:403–417
- 3. Lauman E, Paik B, Rosen R. Sexual dysfunction in the United States: prevalence, predictors and outcomes. JAMA 1999;281:537–544
- Fedele D, Bortolotti A, Coscelli C, Santeusanio F, Chatenoud L, Colli E, Lavezzari M, Landoni M, Parazzini F, on behalf of Gruppo Italiano Studio Deficit Erettile nei Diabetici. Erectile dysfunction in type 1 and type 2 diabetics in Italy. Int J Epide-

miol 2000;29:524-531

- Rhodenet EL, Ribeiro EP, Riedner CE, Teloken C, Souto CA. Glycosylated haemoglobin levels and the severity of erectile function in diabetic men. BJU Int 2005; 95:615–617
- Enzlin P, Mathieu C, Vanderschueren D, Demyttenaere K. Diabetes mellitus and female sexuality: a review of 25 years' research (Review). Diabet Med 1998; 15:809–815
- Rosen L, Rosen RC. Fifty years of FSD research and concepts: from Kinsey to the present. In Women's Sexual Function and Dysfunction: Study, Diagnosis and Treatment. Goldstein I, Meston C, Davis S, Traish A, Eds. New York, Taylor & Francis, 2006, p. 3–10
- Althof SE, Rosen RC, DeRogatis L, Corty E, Quirk F, Symonds T. Outcome measurement in female sexual dysfunction clinical trials: review and recommendations. J Sex Marital Ther 2005;31:153– 166
- Enzlin P, Mathieu C, Van den Bruel A, Bosteels J, Vanderschueren D, Demyttenaere K. Sexual dysfunction in women with type 1 diabetes: a controlled study. Diabetes Care 2002;25:672–677
- Enzlin P, Mathieu C, Van Den Bruel A, Vanderschueren D, Demyttenaere K. Prevalence and predictors of sexual dysfunction in patients with type 1 diabetes. Diabetes Care 2003;26:409–414
- 11. The Diabetes Control and Complications Trial (DCCT). Design and methodologic considerations for the feasibility phase: the DCCT Research Group. Diabetes 1986;35:530–545
- The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med 1993;329: 977–986
- EDIC Research Group. Epidemiology of Diabetes Interventions and Complications (EDIC): design, implementation, and preliminary results of a long-term follow-up of the Diabetes Control and Complications Trial cohort. Diabetes Care

1999;22:99-111

- 14. Steffes M, Cleary P, Goldstein D, Little R, Wiemeyer H, Rohlfing C, England J, Bucksa J, Norwicki M, the DCCT Research Group. Hemoglobin A1c measurements over nearly two decades: sustaining comparable values throughout the Diabetes Control and Complications Trial and the Epidemiology of Diabetes Interventions and Complications study. Clin Chem 2005;51:753–758
- Rosen RC, Brown C, Heiman J, Leiblum S, Meston CM, Shabsigh R, Ferguson D, D'Agostino R. The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. J Sex Marital Ther 2000;26:191–208
- Meston CM. Validation of the Female Sexual Function Index (FSFI) in women with female orgasmic disorder and in women with hypoactive sexual desire disorder. J Sex Marital Ther 2003;29:39–46
- 17. Masheb RM, Lozano-Blanco C, Kohorn EI, Minkin MJ, Kerns RD. Assessing sexual function and dyspareunia with the Female Sexual Function Index (FSFI) in women with vulvodynia. J Sex Marital Ther 2004;30:315–324
- Wiegel M, Meston C, Rosen R. The female sexual function index (FSFI): cross-validation and development of clinical cutoff scores. J Sex Marital Ther 2005;31:1–20
- Jensen SB. Sexual relationships in couples with a diabetic partner. J Sex Marital Ther 1985;11:259–270
- Laan E, Everaerd W, van Berlo R, Rijs L. Mood and sexual arousal in women. Behav Res Ther 1995;33:441–443
- 21. Basson R. Human sex-response cycles. J Sex Marital Ther 2001;27:33–43
- 22. Chivers ML, Bailey JM. A sex difference in features that elicit genital response. Biol Psychol 2005;70:115–120
- Schreiner-Engel P. Diabetes mellitus and female sexuality. Sex Disabil 1983;6: 83–92
- 24. Wincze JP, Albert A, Bansal S. Sexual arousal in diabetic females: physiological and self-report measures. Arch Sex Behav 1993;22:587–601