Longitudinal Assessment of Quality of Life in Patients With Type 2 Diabetes and Self-Reported Erectile Dysfunction

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OBJECTIVE — In the context of the QuED (Quality of Care and Outcomes in Type 2 Diabetes) project, we evaluated the longitudinal changes over 3 years in quality of life (QoL) in patients with type 2 diabetes according to the presence or the development of erectile dysfunction (ED).

RESEARCH DESIGN AND METHODS — Patients were requested to fill in a questionnaire investigating the presence of ED and QoL (SF-36 Health Survey, depression symptoms [Center for Epidemiologic Studies–Depression], and quality of sexual life) every 6 months for 3 years. The analyses were based on multilevel models, adjusted for patient clinical and sociodemographic characteristics.

RESULTS — The study involved 1,456 patients, of whom 34% reported frequent erectile problems at baseline; 192 developed ED during the follow-up. No changes in QoL measures were detected in patients without ED; in those with ED at baseline, a worsening in all SF-36 scales was observed, reaching statistical significance for physical functioning ($P = 0.03$). Among patients who developed ED during the study, a deterioration in all SF-36 dimensions and a worsening in depressive symptoms preceded the development of ED. The onset of ED was associated with a further marked worsening in physical functioning ($P = 0.0008$), general health perception ($P = 0.02$), and social functioning ($P = 0.04$) on SF-36 subscales, as well as in the summary physical and mental components scores ($P = 0.04$ and $P = 0.07$, respectively). The development of ED was also associated with a highly significant increase in depressive symptoms ($P = 0.001$) and a marked decrease in quality of sexual life ($P < 0.0001$).

CONCLUSIONS — This longitudinal study documents for the first time the impact of ED onset on several aspects of QoL in patients with type 2 diabetes. The study also shows that QoL tended to further decrease during 3 years in patients with ED at baseline but not in those without this condition.

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Erectile dysfunction (ED) has a broad negative impact on health-related quality of life (QoL) in patients with type 2 diabetes (1). An international multicenter disease registry of men with ED has also shown that diabetic men with ED appear to have more severe dysfunction than nondiabetic men with ED and also present with worse disease-specific health-related QoL (2).

Most of the information about the impact of ED on QoL comes from cross-sectional studies involving the general population (3–5). Information on patients with diabetes is extremely scarce (1,2), particularly that describing the trend over time of QoL in patients with ED (2); furthermore, no data are available regarding the changes in QoL produced by the onset of ED.

In the context of the QuED (Quality of Care and Outcomes in Type 2 Diabetes) project we have previously documented the fact that patients with ED at study entry had a significantly worse QoL compared with those not suffering from this complication (1). The aim of this study was to describe the longitudinal changes over 3 years in QoL scores in patients who developed ED during the study and in those who already had ED at study entry.

RESEARCH DESIGN AND METHODS

— The study design has already been described in detail elsewhere (1). Briefly, physicians were identified in all regions of Italy and selected according to their willingness to participate in the project. Overall, 114 diabetes outpatient clinics and 112 general practitioners participated in the study.

All patients with type 2 diabetes were considered eligible for this project, irrespective of age, duration of diabetes, and treatment. In diabetes outpatient clinics, patients were sampled by using random lists, stratified by patient age (<65 or ≥65 years). Each center was asked to recruit at least 30 patients, whereas general practitioners enrolled only those patients for whom they were primarily responsible for diabetes care. Clinical information was abstracted from clinical records by the participating physicians and reported in ad hoc forms. Data were collected at baseline and at 6-month intervals for 3 years.

Baseline clinical variables referred to the last value in the previous 12 months. Because normal ranges for HbA_{1c} varied among the different centers, the percentage change with respect to the upper normal value (actual value/upper normal limit) was estimated and multiplied by 6.0. Cardiovascular disease (CVD) included myocardial infarction, angina,

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Abbreviations: CES-D, Center for Epidemiologic Studies–Depression; CVD, cardiovascular disease; ED, erectile dysfunction; QoL, quality of life; TIBI, Total Illness Burden Index.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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coronary revascularization procedures, stroke, and lower limb complications (claudication, ulcer, gangrene, amputation, and aortic-femoral revascularization procedures).

All subjects were asked to complete a questionnaire upon entry into the study and at 6-month intervals over a period of 3 years. The questionnaire was self-administered and then sent anonymously to the coordinating center in prepaid envelopes. The matching between clinical data and the questionnaire was made possible through a code put by the physician on both sources of information. No other details on patient identity were contained neither in the questionnaire nor in clinical data.

The presence of ED was investigated by asking the patient how often he had experienced problems in achieving and maintaining an erection during the past 6 months, with responses calibrated on a 5-level scale (from never to more than once per week). We considered only those patients who reported frequent erectile problems (almost every week or more than once a week) as being affected by ED. Incident cases of ED were considered those patients without ED at baseline who reported frequent erectile problems during the follow-up. The presence and severity of diabetes complications and comorbidities were summarized by using the Total Illness Burden Index (TIBI), a widely used comorbidity measure specifically developed for outpatient populations (6).

QoL

QoL was assessed using the SF-36 Health Survey, a generic measure covering eight dimensions: physical functioning, role limitations caused by physical health problems, bodily pain, general health perception, vitality, social functioning, role limitations caused by emotional health problems, and mental health (7). Scores on all the subscales are transformed linearly to a possible range of 0–100; higher scores indicated more favorable physical functioning/psychological well-being. These eight domains may be further aggregated into two summary measures: the physical component summary measure and the mental component summary measure (8).

Depressive symptoms

The Center for Epidemiologic Studies–Depression (CES-D) Scale is a self-reported measure of depression composed of 20 items addressing symptoms of depression during the previous 4 weeks. Values of the CES-D Scale range from 0 to 60 with higher values indicating more severe depressive symptoms (9).

Quality of sexual life

We evaluated the quality of sexual life using the Sexual Life Questionnaire composed of six items. The score ranges between 0 and 100, with higher values indicating better quality of sexual life. Details on the questionnaire validation have been reported in a previous paper (1).

Statistical analysis

Patients' characteristics according to the presence/development of ED were compared using the χ^2 test for categorical variables and the Mann-Whitney *U* test for continuous variables. Changes in QoL scores during the study were calculated as the difference between baseline and last follow-up value and compared using the paired *t* test. Effect sizes were calculated by dividing the changes in each QoL score by the SD of that score estimated at baseline on the entire sample.

To account for the hierarchical nature of the data (repeated measurements within patients) and to control simultaneously for the possible confounding effects of the different variables, we utilized multivariate multilevel linear models (10,11). In our longitudinal analysis, which evaluated factors associated with a decline in QoL measures, multilevel methods allowed to appropriately model within- and between-patient variability (12).

Among baseline patient characteristics, the following sociodemographic and clinical characteristics were considered: age, school education, marital status, diabetes duration, previous history of a cardiovascular event, diabetes therapy, hypertension, presence, and severity of comorbidity (TIBI). We considered the occurrence of ED and the incidence of CVD events during the follow-up as time-dependent covariates.

Results are expressed in terms of standardized β parameters with the relative *P* value. Standardized β parameters indicate the changes over time in QoL measures with respect to baseline for patients without ED and those with ED at baseline. For patients who developed ED during the follow-up, the β parameters show the average change from before to after the development of ED. All the analyses were performed using SAS Statistical Package, version 8.2 (13).

RESULTS — The study involved 1,456 patients, of whom 500 patients (34%) reported frequent erectile problems at study entry and 192 patients (13.2%) developed ED during the follow-up. Patients' characteristics according to the presence or development of ED are reported in Table 1. Patients who developed ED were older; had longer duration of diabetes, worse metabolic control, and a higher TIBI score; and were more often treated with insulin and affected by hypertension, neuropathy, micro- or macroalbuminuria, or CVD compared with those without ED. With respect to patients with ED at baseline, those who developed ED during the follow up were less often treated with insulin, less likely to have retinopathy, and showed a lower TIBI score.

The analysis of QoL scores during 3 years of follow-up showed that no major changes were present among patients without ED, except for a slight improvement in depressive symptoms ($P = 0.016$) (Table 2). In individuals with ED at baseline we documented a worsening in the physical dimensions of the SF-36, which reached the statistical significance for physical functioning ($P = 0.003$) and the physical component summary measure ($P = 0.008$). Among men who developed ED during the follow up, all the QoL measures showed a deterioration, reaching statistical significance for physical functioning ($P = 0.04$), the physical component summary measure ($P = 0.018$), and quality of sexual life ($P < 0.0001$).

Patterns of QoL measures from 24 months before the onset of ED to 18 months after the onset of ED are displayed in Fig. 1. For all the SF-36 dimensions, a deterioration in QoL seems to precede the development of ED. In particular, in looking at the physical and mental components summary measures, the deterioration in the physical domain seems to precede by 6 months the decrease in the psychological well-being. The onset of ED is clearly associated with a further decrease in all the scores, which reach the lowest level concomitantly with its occurrence. Similarly, a worsening of depressive symptoms precedes the onset of ED, reaches its highest level concomitantly with it, and tends to plateau thereafter. As expected, erectile problems are associated with a steep decline in the quality of sexual life.

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Table 1—*Patients' characteristics according to the presence/development of ED*

Characteristics	ED			*P**	*P*†
	No	At baseline	Incident		
n	764 (52.5)	500 (34.3)	192 (13.2)		
Age (years)	58.9 ± 10.4	65.0 ± 8.2	64.3 ± 7.8	<0.0001	0.17
School education ≤5 years	39.1	30.8	40.6	0.71	0.01
Income				0.44	0.54
<€6.000	6.2	7.4	7.1		
€6–12.000	31.2	31.0	35.5		
>€12.000	62.6	61.6	57.4		
Smoking				0.13	0.55
No	26.0	21.1	20.4		
Yes	26.1	19.8	23.7		
Ex	47.9	59.1	55.9		
BMI (kg/m^2)	27.5 ± 3.7	27.3 ± 7.2	27.3 ± 7.3	0.57	0.98
Diabetes duration (years)	8.6 ± 7.6	12.5 ± 9.3	11.7 ± 9.0	<0.0001	0.38
Diabetes treatment				0.04	0.01
Diet alone	23.1	9.3	18.2		
Oral agents	64.2	64.4	61.5		
Insulin	7.9	15.9	11.5		
Insulin + oral agents	4.8	10.4	8.9		
HbA_{1c} (%)	6.9 ± 1.5	7.2 ± 1.6	7.3 ± 1.7	0.004	0.60
Retinopathy	13.9	28.4	19.4	0.07	0.02
Neuropathy	5.1	15.7	14.3	<0.0001	0.66
Micro- or macroalbuminuria	19.7	29.7	29.0	0.02	0.89
Hypertension	39.3	50.2	50.0	0.007	0.96
Dyslipidemia	20.0	20.6	19.3	0.81	0.70
Peripheral vascular disease	3.4	5.4	4.2	0.61	0.51
CVD	12.8	24.8	19.8	0.01	0.16
TIBI	9.8 ± 9.8	15.4 ± 12.4	12.3 ± 10.6	0.0006	0.005

Data are *n* (%), %, or means ± SD. *P* values refer to χ^2 for categorical variables and Mann-Whitney *U* test for continuous variables. *Incident ED versus no ED. †Incident ED versus ED at baseline.

Multilevel models confirmed that no changes in QoL measures were detected during 3 years in men without ED, with the only exception being a marginally significant improvement in the social functioning SF-36 subscale (Table 3).

Among patients with ED at baseline, a worsening in all SF-36 scales was observed, even though statistical significance was reached for physical functioning only. The severity of depressive symptoms also slightly increased. On the other hand, the quality of sexual life score tended to improve (Table 3).

Among the patients who developed ED during the study, this condition was associated with a marked worsening in the physical functioning, general health perception, and social functioning SF-36 subscales as well as in the summary physical component score. The development of ED was also associated with a highly significant increase in depressive symptoms and a marked decrease in quality of sexual life (Table 3).

Among the other variables investigated, the severity of diabetes and its complications as summarized by the TIBI and the presence of CVD represented the strongest predictors of decline in all the scales. Low levels of school education and older age also predicted a worsening in the physical components of SF-36 (Table 3).

CONCLUSIONS — A few cross-sectional studies have described the association between the presence of ED and

Table 2—*Changes in QoL measures from baseline to last follow-up according to the presence/development of ED*

QoL measures	ED								
	No			At baseline			Incident		
	Baseline	Change*	Effect size	Baseline	Change*	Effect size	Baseline	Change*	Effect size
PF	84.7 ± 17.7	0.3 ± 16.7	0.01	75.1 ± 23.3	**−3.3 ± 20.1**	−0.16	76.3 ± 23.3	**−3.5 ± 24.1**	−0.16
RP	77.4 ± 34.6	−0.8 ± 39.2	−0.02	58.0 ± 43.1	−0.7 ± 40.6	−0.02	60.5 ± 41.0	−1.6 ± 43.9	−0.04
BP	78.0 ± 23.5	−0.2 ± 25.9	−0.08	67.1 ± 25.6	−1.2 ± 25.7	−0.05	70.4 ± 26.1	0.4 ± 29.6	0.01
GH	61.6 ± 18.0	0.5 ± 16.4	0.02	51.7 ± 20.2	−1.3 ± 16.7	−0.06	55.4 ± 19.6	−2.2 ± 20.2	−0.11
VT	67.2 ± 18.1	0.1 ± 16.5	0.005	56.7 ± 20.0	−0.9 ± 17.6	−0.04	59.5 ± 18.8	−2.3 ± 18.5	−0.12
SF	78.8 ± 21.8	1.1 ± 24.1	0.05	67.0 ± 26.1	2.0 ± 24.7	0.08	72.5 ± 23.1	−1.2 ± 28.0	−0.05
RE	78.1 ± 34.6	2.5 ± 39.8	0.06	59.2 ± 43.2	2.1 ± 40.7	0.05	62.5 ± 40.8	−2.0 ± 48.4	−0.05
MH	73.5 ± 18.3	0.5 ± 16.1	0.02	65.0 ± 21.3	1.0 ± 16.9	0.05	68.1 ± 17.3	−2.2 ± 18.6	−0.11
PCS	49.3 ± 7.6	−0.2 ± 7.3	−0.02	44.7 ± 8.6	**−1.0 ± 7.3**	−0.12	46.8 ± 8.5	**−1.4 ± 9.3**	−0.16
MCS	49.0 ± 10.0	0.8 ± 9.4	0.07	44.6 ± 11.6	1.0 ± 9.9	0.10	46.3 ± 9.5	−1.1 ± 10.6	−0.10
SLQ	84.3 ± 16.4	0.7 ± 14.7	0.03	62.1 ± 23.2	−0.3 ± 23.1	−0.01	75.5 ± 20.9	**−8.5 ± 20.2**	−0.39
CES-D	16.3 ± 9.0	**−0.8 ± 8.0**	−0.09	19.9 ± 10.0	0.6 ± 9.1	0.07	18.7 ± 8.9	1.0 ± 9.6	0.10

Statistically significant changes from baseline ($P \leq 0.05$) are in boldface. *Positive change indicates improvement for SF-36 dimensions and Sexual Life Questionnaire (SLQ) and deterioration for CES-D score; negative change indicates deterioration for SF-36 dimensions and SLQ and improvement for CES-D score. BP, bodily pain; GH, general health perception; MCS, mental component summary; MH, mental health; PCS, physical component summary; PF, physical functioning; RE, role limitations caused by emotional health problems; RP, role limitations caused by physical health problems; SF, social functioning; VT, vitality.

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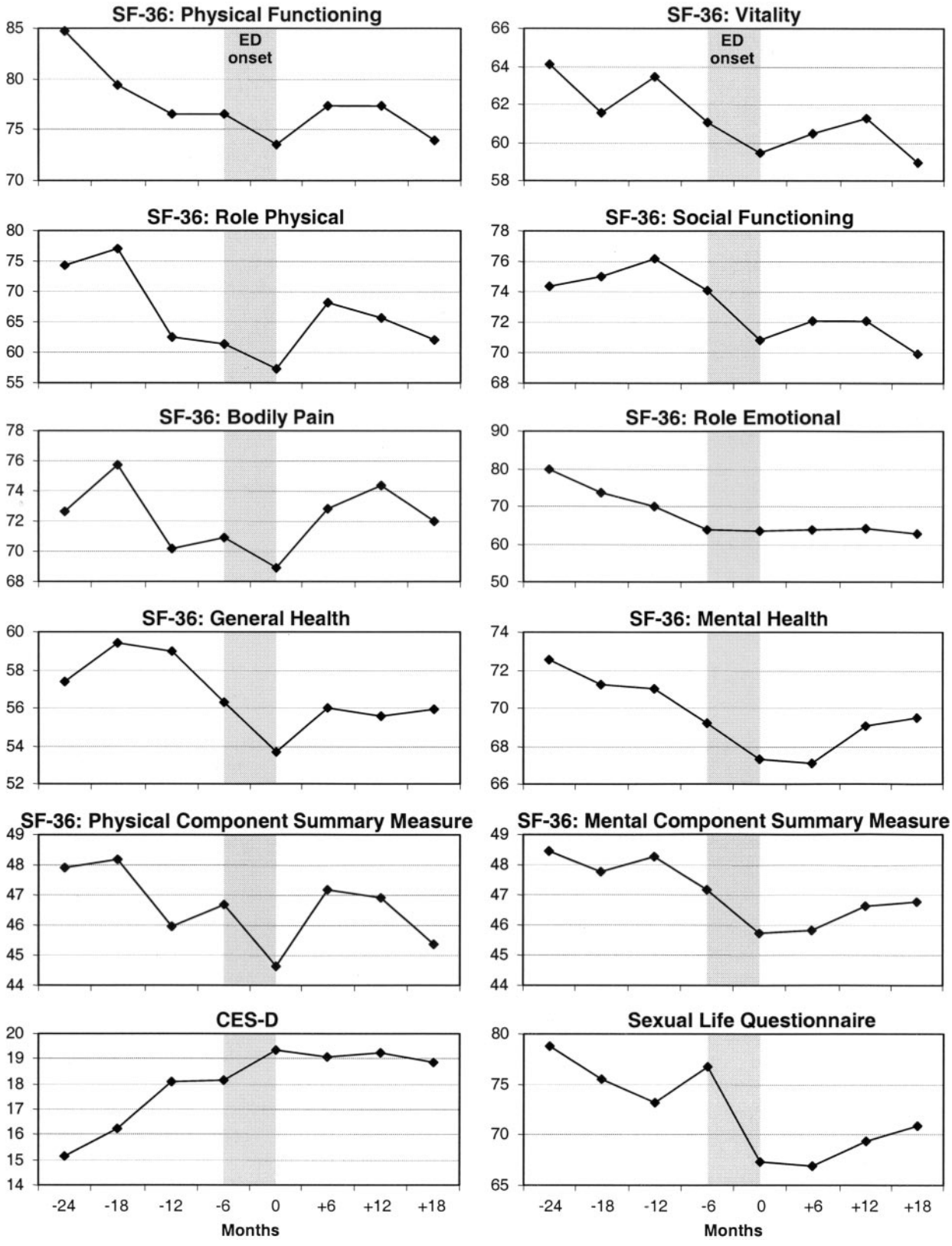

Figure 1—*Patterns of QoL measures from 24 months before to 18 months after the onset of ED.*

poorer QoL (1–5); nevertheless, no long-term, longitudinal evaluation of the impact of this condition on physical and psychological well-being is available. We describe for the first time changes in QoL occurring over 3 years in men with type 2 diabetes and ED and the deterioration in QoL subsequent to the development of ED.

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Table 3—*Independent predictors of longitudinal changes in QoL scores: results of multilevel analyses*

	SF-36							
Covariates	PF	RP	BP	GH	VT	SF	RE	MH
No ED	0.44 (0.66)	0.75 (0.46)	0.16 (0.88)	−0.75 (0.45)	−0.61 (0.54)	2.00 (0.05)	1.08 (0.28)	0.36 (0.72)
ED at baseline	−2.22 (0.03)	−0.96 (0.34)	−0.83 (0.41)	−0.54 (0.59)	−1.20 (0.23)	−0.55 (0.58)	−0.85 (0.40)	−0.20 (0.84)
Incident ED	−3.36 (0.0008)	−1.24 (0.22)	−1.11 (0.27)	−2.43 (0.02)	−1.14 (0.25)	−2.07 (0.04)	−1.24 (0.21)	−1.45 (0.15)
Age	−8.73 (<0.0001)	−8.72 (<0.0001)	−3.28 (0.001)	0.98 (0.33)	2.93 (0.003)	0.70 (0.48)	−4.26 (<0.0001)	4.55 (<0.0001)
Marital status (single/ divorced/ widowed vs. married)	−0.95 (0.34)	−2.07 (0.04)	−1.73 (0.08)	−2.51 (0.01)	−1.77 (0.08)	−1.86 (0.06)	−2.82 (0.005)	−1.23 (0.22)
School education (≤5 years vs. >5 years)	−6.48 (<0.0001)	−4.26 (<0.0001)	−4.68 (<0.0001)	−2.76 (0.006)	−1.85 (0.06)	−0.69 (0.49)	−2.70 (0.007)	−0.93 (0.35)
Diabetes duration	0.66 (0.51)	0.53 (0.60)	−1.62 (0.11)	−4.06 (<0.0001)	−2.31 (0.02)	−2.47 (0.01)	1.32 (0.19)	−1.49 (0.14)
Treatment								
Insulin vs. diet/ OA	−3.33 (0.0009)	−2.05 (0.04)	−0.07 (0.95)	−3.47 (0.0005)	−1.23 (0.22)	−2.22 (0.03)	−0.95 (0.34)	−1.20 (0.23)
OA + insulin vs. diet/OA	−0.88 (0.38)	−2.09 (0.04)	−2.11 (0.03)	−1.75 (0.08)	−0.09 (0.92)	−1.76 (0.08)	−1.45 (0.15)	−0.38 (0.70)
TIBI	−14.12 (<0.0001)	−11.12 (<0.0001)	−16.32 (<0.0001)	−11.33 (<0.0001)	−15.35 (<0.0001)	−11.21 (<0.0001)	−10.88 (<0.0001)	−11.61 (<0.0001)
CVD at baseline	−5.81 (<0.0001)	−4.00 (<0.0001)	−1.87 (0.06)	−2.97 (0.003)	−3.76 (0.0002)	−1.87 (0.06)	−2.87 (0.0004)	−2.40 (0.02)
CVD at follow-up	−1.86 (0.06)	−2.22 (0.03)	−1.48 (0.14)	−2.73 (0.006)	0.25 (0.81)	−1.18 (0.24)	−1.25 (0.21)	1.34 (0.18)

Data are standardized β (*P* value). Standardized β parameters indicate the changes over time in QoL measures with respect to baseline. Positive standardized β parameters indicate improvement for SF-36 dimensions and Sexual Life Questionnaire (SLQ) and deterioration for CES-D score; negative standardized β parameters indicate deterioration for SF-36 dimensions and SLQ and improvement for CES-D score. The impact of ED is partitioned in two components: the first indicates the changes over time in patients with ED at baseline; the second shows the average changes before to after the development of ED. BP, bodily pain; GH, general health perception; MCS, mental component summary; MH, mental health; OA, oral agent; PCS, physical component summary; PF, physical functioning; RE, role limitations caused by emotional health problems; RP, role limitations caused by physical health problems; SF, social functioning; VT, vitality.

In our study, QoL remained substantially unchanged among patients without erectile problems, whereas men with ED at baseline showed a significant deterioration in physical functioning. This finding can be related to the more severe clinical conditions of these patients, who show a markedly higher prevalence of micro- and macrovascular complications, as well as significantly older age. It is interesting to note that men with ED at baseline showed a statistically significant improvement in the quality of their sexual life. A noteworthy occurrence is that sildenafil became available on the market in Italy in 1998, concomitantly with the collection of the baseline data for our study. Therefore, although we do not have information about the use of this drug, it is reasonable to assume that such an improvement may be at least partially related to the availability of new effective oral treatments for ED.

The study offered a unique opportunity to evaluate QoL in patients with type 2 diabetes before and after the onset of ED. From a clinical point of view, men who developed ED during the follow-up had more severe clinical conditions at baseline compared with those without ED but very similar to those who had already reported erectile problems at study entry. These findings suggest that the presence of ED should be regularly investigated in patients with type 2 diabetes of longer duration, particularly when associated with micro- and macrovascular complications.

Patterns of QoL scores before and after the onset of ED suggest that a deterioration in physical well-being, followed by a worsening in psychological well-being, precede the development of sexual problems, thus suggesting an interplay between clinical and psychological factors in determining ED. Such a decline in QoL was not attributable to the incidence of new CVD events; in fact, only 8 of 192 patients who developed ED during the study also experienced a CVD event before ED onset. An alternative explanation for these findings could be represented by the occurrence of subtle pathological changes affecting the biopsychosocial functioning of the patient before manifestation of objective signs.

Erectile problems further deteriorate a patient's health perception: for all the aspects investigated a worse score was reached concomitantly with the reporting of erectile problems. These findings were confirmed by multilevel analyses suggesting a greater impact of ED on physical functioning, depressive symptoms, general health perception, and social functioning. As expected, the dimension of QoL more seriously affected was represented by quality of sexual life, showing a dramatic decline as a consequence of ED onset.

Our data underline the importance of monitoring patients' physical and emotional well-being: a deterioration in these aspects of QoL can represent an alarm bell for the development of sexual problems that will further contribute to worsen subjective health perception. Because patients could be reluctant to discuss their sexual problems, physicians should actively investigate these aspects in the light of the availability of effective treatments. In this regard, several studies have shown

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Table 3—*Continued*

SF-36 summary scores			
PCS	MCS	CES-D	SLQ
−1.22 (0.22)	1.48 (0.14)	−0.81 (0.42)	−0.06 (0.95)
−1.21 (0.22)	−0.46 (0.65)	0.86 (0.39)	2.41 (0.02)
−2.08 (0.04)	−1.81 (0.07)	3.22 (0.001)	−8.00 (<0.0001)
−8.02 (<0.0001)	4.68 (<0.0001)	−1.09 (0.28)	0.03 (0.97)
−1.52 (0.13)	−1.90 (0.06)	4.70 (<0.0001)	−0.35 (0.73)
−5.71 (<0.0001)	0.07 (0.94)	1.01 (0.31)	1.01 (0.31)
−1.17 (0.24)	−1.18 (0.24)	0.44 (0.66)	−3.22 (0.001)
−2.83 (0.005)	−0.72 (0.47)	0.83 (0.41)	−2.63 (0.009)
−2.79 (0.0005)	−0.71 (0.48)	1.47 (0.14)	0.16 (0.87)
−16.38 (<0.0001)	−10.44 (<0.0001)	11.06 (<0.0001)	−8.78 (<0.0001)
−5.24 (<0.0001)	−1.55 (0.12)	1.48 (0.14)	−1.84 (0.07)
−3.30 (0.001)	0.26 (0.80)	−0.36 (0.72)	−0.23 (0.82)

the positive effects of therapy on different aspects of QoL (14–17).

Two potential methodological limitations of our study need to be discussed. The presence of ED was based on patient self-report, without any attempt to clinically confirm the diagnosis. Nevertheless, subjective evaluation of the individual's erection and satisfaction for sexual life are more likely to influence psychological well-being rather than the objective evaluation of the degree of ED. Second, we had no information on the use of treatment for ED after its diagnosis. Therefore, QoL scores after the onset of ED could have been at least partially influenced by such therapies and the impact of ED could be even greater than that documented.

In summary, this longitudinal study documents for the first time the impact of the onset of ED on several aspects of QoL in patients with type 2 diabetes. The study also shows that QoL tended to further decrease during 3 years in patients with ED at baseline, but not in those without this condition.

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APPENDIX

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References

1. De Berardis G, Franciosi M, Belfiglio M, Di Nardo B, Greenfield S, Kaplan SH, Pellegrini F, Sacco M, Tognoni G, Valentini M, Nicolucci A; Quality of Care and Outcomes in Type 2 Diabetes (QuED) Study Group: Erectile dysfunction and quality of life in type 2 diabetic patients: a serious problem too often overlooked. *Diabetes Care* 25:284–291, 2002
2. Penson DF, Latini DM, Lubeck DP, Wallace KL, Henning JM, Lue TF: Do impotent men with diabetes have more severe erectile dysfunction and worse quality of life than the general population of impotent patients? Results from the Exploratory Comprehensive Evaluation of Erectile Dysfunction (ExCEED) database. *Diabetes Care* 26:1093–1099, 2003
3. Sanchez-Cruz JJ, Cabrera-Leon A, Martin-Morales A, Fernandez A, Burgos R, Rejas J: Male erectile dysfunction and health-related quality of life. *Eur Urol* 44:245–253, 2003
4. Guest JF, Das Gupta R: Health-related quality of life in a UK-based population of men with erectile dysfunction. *Pharmacoeconomics* 20:109–117, 2002
5. Litwin MS, Nied RJ, Dhanani N: Health-related quality of life in men with erectile dysfunction. *J Gen Intern Med* 13:159–166, 1998
6. Greenfield S, Sullivan L, Dukes KA, Silliman R, D'Agostino R, Kaplan SH: Development and testing of a new measure of case mix for use in office practice. *Med Care* 33 (Suppl.):AS47–AS55, 1995
7. Ware J, Snow K, Kosinski M, Gandek B: *SF-36 Health Survey: Manual and Interpretation Guide*. Boston, The Health Institute, New England Medical Center, 1993
8. Ware JE, Kosinski M, Keller SD: *SF-36 Physical and Mental Health Summary Scales: A User's Manual*. Boston, The Health Institute, New England Medical Center, 1994
9. Radloff LS: The CES-D scale: a self-report depression scale for research in the general population. *Appl Psychol Meas* 1:385–401, 1977
10. Snijders TAB, Bosker RJ: *Multilevel Analysis: An Introduction to Basic and Advanced Multilevel Modeling*. London, SAGE, 1999
11. Sullivan LM, Dukes KA, Losina E: Tutorial in biostatistics: an introduction to hierarchical linear modelling. *Stat Med* 18: 855–888, 1999
12. DeLong E: Hierarchical modeling: its time has come. *Am Heart J* 145:16–18, 2003
13. *SAS Language*. Version 8.2. Cary, NC, SAS Institute, 2001
14. Fujisawa M, Sawada K, Okada H, Arakawa S, Saito S, Kamidono S: Evaluation of health-related quality of life in patients treated for erectile dysfunction with viagra (sildenafil citrate) using SF-36 score. *Arch Androl* 48:15–21, 2002
15. Giuliano F, Pena BM, Mishra A, Smith MD: Efficacy results and quality-of-life measures in men receiving sildenafil citrate for the treatment of erectile dysfunction. *Qual Life Res* 10:359–369, 2001
16. Willke RJ, Yen W, Parkerson GR Jr, Linet OI, Erder MH, Glick HA: Quality of life effects of alprostadil therapy for erectile dysfunction: results of a trial in Europe and South Africa. *Int J Impot Res* 10:239–246, 1998
17. Williams G, Abbou CC, Amar ET, Desvaux P, Flam TA, Lycklama A, Nijeholt GA, Lynch SF, Morgan RJ, Muller SC, Porst H, Pryor JP, Ryan P, Witzsch UK, Hall MM, Place VA, Spivack AP, Todd LK, Gesundheit N: The effect of transurethral alprostadil on the quality of life of men with erectile dysfunction, and their partners: MUSE Study Group. *Br J Urol* 82: 847–854, 1998

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