Quality of Life Outcomes in Patients With Obsessive-Compulsive Disorder: Relationship to Treatment Response and Symptom Relapse

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Objective: Data were analyzed from 2 prospective, double-blind, placebo-controlled trials of escitalopram in obsessive-compulsive disorder (OCD) to characterize the baseline levels of functional disability and impairment in health-related quality of life (HRQoL) and to assess the relationship between treatment outcomes (response or relapse) and disability or HRQoL.

Method: Data from a 24-week, placebo-controlled, fixed-dose trial (N = 466) of escitalopram (10–20 mg/d) or paroxetine (40 mg/d) and from a 40-week, flexible-dose (escitalopram 10–20 mg/d), placebo-controlled relapse-prevention trial (N = 468) were analyzed. Obsessive-compulsive disorder symptoms (*DSM-IV* criteria) were assessed using the Yale-Brown Obsessive Compulsive Scale (YBOCS), functioning was assessed using the Sheehan Disability Scale (SDS), and HRQoL was assessed using the Medical Outcomes Study Short Form (SF-36). Baseline data were pooled for patients across both studies. For patients in the fixed-dose study, SDS and SF-36 scores were compared across treatment groups and for responders versus nonresponders. In the relapse-prevention trial, SDS and SF-36 scores were compared for relapsed versus nonrelapsed patients.

Results: Patients with more severe baseline symptoms (YBOCS ≥ 27) reported significantly greater impairment on the SDS ($P < .001$) and SF-36 (except for bodily pain). Patients receiving escitalopram or paroxetine reported significant improvements on most SF-36 dimensions and on the SDS compared to placebo; however, improvements in work-related functioning were seen earlier for patients receiving escitalopram (20 mg/d). At the study endpoints, SDS and SF-36 scores were significantly better for patients who were responders (versus nonresponders) and for patients who did not relapse (versus relapsers).

Conclusions: Obsessive-compulsive disorder is associated with significant impairment in functioning and HRQoL. Significant differences in disability and HRQoL between responders and nonresponders or relapsers and nonrelapsers suggest a relationship between symptomatic and functional outcomes.

Trial Registration: lundbecktrials.com Identifiers: 10205 and 10193

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Obsessive-compulsive disorder (OCD) is a chronic condition affecting 1%–3% of the population.[1–3] Patients with OCD can suffer from considerable disability across a broad range of functional and health-related quality of life (HRQoL) domains, which impairs professional and socioeconomic status, as well as family relations.[2,4–9] Greater impairment in family life and activities of daily living has been reported in patients with OCD compared to those with social anxiety disorder and panic disorder.[7] Overall, the degree of social impairment in OCD patients may be comparable to that of patients with schizophrenia.[10,11]

Functional disability and diminished HRQoL are documented but not well characterized in patients with OCD. To date, the association between OCD symptoms and functional or HRQoL outcomes has been examined in a handful of studies. These studies provide evidence for functional and HRQoL improvements in response to OCD treatment, although the relationship with symptom improvements is not clear.[12–16] For instance, studies by Tenney and colleagues[16] and Norberg and colleagues[15] suggest a degree of incongruence between symptom and HRQoL improvements, in at least some patients. This incongruence may reflect any number of methodological variables, including the choice of functional and HRQoL scales or type of clinical intervention. In some cases, functional improvements in the absence of treatment response may reflect an improvement in comorbid symptoms, such as depression. It is also possible that functional and HRQoL improvements follow a more protracted time-course than symptom improvements. Indeed, in patients with major depression, delays between symptom improvements and appreciable improvements in function have been noted.[17,18] If such a delay exists in OCD patients, then a consistent relationship between symptom improvements and improvements in function or HRQoL may be observed only after longer treatment periods.

Clinical trials designed to assess the efficacy of OCD treatments generally focus on symptom rating scales such as the Yale-Brown Obsessive Compulsive Scale (YBOCS).[19] Pharmacotherapy with serotonin reuptake inhibitors, including both selective serotonin reuptake inhibitors (SSRIs) and the tricyclic serotonin reuptake inhibitor clomipramine, can reduce YBOCS scores and improve categorical outcomes based on the YBOCS, such as response and remission rates, as well as decrease relapse rates.[20–22] An unresolved issue concerns the extent to which symptom improvements assessed using the YBOCS translate into clinically meaningful improvements in functioning and quality of life. From a slightly different perspective, the issue may be viewed as whether or

not categorical outcomes defined by YBOCS criteria can be clinically validated using measures of disability, functioning, or quality of life.[23] One of the first challenges in addressing this issue is to identify measures of disability or HRQoL that are sensitive to symptom change in patients with OCD.

Two long-term efficacy trials have been conducted with escitalopram: 1 was a 24-week fixed-dose parallel study that included both a placebo and an active SSRI (paroxetine) control group,[24] and the other was a 40-week placebo-controlled relapse prevention study.[25] Each of these studies included prospective assessments of efficacy (YBOCS), function (Sheehan Disability Scale; SDS),[26] and HRQoL (Medical Outcomes Study Short Form; SF-36).[27] Both the SDS and the SF-36 have been used as outcome measures in patients with OCD and have been shown in modest-sized trials to be sensitive to symptom improvement.[12,28–30] Data from these 2 trials afford a unique opportunity to assess functional and HRQoL outcomes in OCD patients. The objectives of the present analyses were to further characterize the relationship between symptom outcomes and functional or HRQoL outcomes, as well as to explore the possibility that functional and HRQoL outcomes can provide a clinically relevant supplement to YBOCS-defined measures of response and relapse.

METHOD

Data on functional outcomes were collected from adult patients participating in either of 2 randomized controlled trials of escitalopram for the treatment of OCD.

Study Design

Functional and HRQoL data were obtained from 2 placebo-controlled trials of escitalopram. One was a placebo-controlled, paroxetine-referenced, fixed-dose, multicenter trial conducted to evaluate the efficacy and tolerability of escitalopram in adult patients with OCD.[24] This study had a 24-week treatment duration with a primary efficacy endpoint after 12 weeks. Patients were randomly assigned to receive fixed doses of escitalopram (10 or 20 mg daily), paroxetine (40 mg daily), or placebo.

The second was a 40-week relapse prevention study in patients with OCD.[25] During the 16-week open-label period, patients received escitalopram 10 mg/d for the first week, after which the dose could be increased to 20 mg/d at a scheduled visit in case of lack of efficacy and could be decreased to 10 mg/d in case of dose-limiting adverse events. After week 12, the dose was fixed. After 16 weeks of treatment, patients with a decrease in YBOCS total score of ≥ 25% relative to baseline were defined as responders and could be randomized in double-blind fashion to continue treatment with escitalopram or to receive placebo for a further 24 weeks.

The trial protocols were approved by local ethics committees, and both trials were conducted in accordance with the International Conference on Harmonization—Good Clinical Practice guidelines and the Declaration of Helsinki. Eligible patients gave their written informed consent prior to participation.

Patients

The inclusion and exclusion criteria were similar in both studies. Criteria for entry into the study were male and female patients aged 18–65 years; a primary diagnosis of *DSM-IV*–diagnosed OCD of at least 1 year's duration, and the OCD had been stable for at least 6 months, according to clinical judgment; a YBOCS score ≥ 20 at screening and baseline; and a Montgomery-Åsberg Depression Rating Scale[31] total score ≤ 22.

Exclusion criteria included comorbid Axis I disorders within the previous 6 months (such as major depressive disorder, panic disorder, generalized anxiety disorder, social anxiety disorder, posttraumatic stress disorder, eating disorders, substance abuse, body dysmorphic disorder, mental retardation, cognitive disorders, schizotypal personality disorder, and tic or pervasive developmental disorders). Patients with a history of bipolar disorder or schizophrenia or other psychotic disorder were excluded from the study. Additional exclusion criteria included a significant personality disorder interfering with assessment, suicide risk (≥ 5 on Montgomery-Åsberg Depression Rating Scale item 10), receiving electroconvulsive therapy or formal psychotherapy, pregnancy, or breast feeding. Patients receiving monoamine-oxidase inhibitors, antidepressants, herbal treatments, serotonergic agonists, or antipsychotics/mood stabilizers were excluded. A history of more than 3 failed SSRI trials was also a contraindication for entry into the study.

Assessments

The YBOCS was used to assess symptom severity and outcomes in both trials. To assess the impact of baseline severity on function and HRQoL, patients were divided into 2 categories: less severe (YBOCS ≤ 26) and more severe (YBOCS ≥ 27). The YBOCS score cut-offs for these categories were based on a median split, with the median baseline YBOCS score for all patients pooled across both studies.

Treatment response was defined as a decrease in YBOCS score of ≥ 25% relative to baseline. In the relapse-prevention study, only patients achieving response to 16 weeks of open-label treatment with escitalopram could be randomized to the double-blind, placebo-controlled relapse-prevention phase. Relapse was defined as an increase in YBOCS total score of ≥ 5 points relative to the score at randomization or an unsatisfactory treatment effect (lack of efficacy) as judged by the investigator.

Health-related quality of life was assessed using the SF-36. This patient-rated questionnaire is designed to assess health or well-being across 8 dimensions: 4 related to mental health (role limitations due to emotional problems, mental health, social functioning, and vitality) and 4 related to physical health (role limitations due to physical problems, physical function, bodily pain, and general health). Scores range from 0 to 100 with higher scores indicating better health.

Disability was assessed using the SDS. This patient-rated scale was designed to assess the level of functioning of psychiatric patients participating in clinical trials. It includes 3 subscales on which patients rate (from 0 to 10, inclusively)

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the extent to which symptoms have disrupted activities related to work or school, social or leisure activities, and family life or home responsibilities.

In the fixed-dose study, the SDS and SF-36 were administered at baseline and at weeks 6, 12, and 24. In the relapse-prevention study, the SDS and the SF-36 were administered at baseline, week 8, and week 16 of the open-label period. During the double-blind, relapse-prevention period, the SDS and SF-36 were administered at 8, 16, and 24 weeks (postrandomization).

Statistical Analysis

Patient population analyses were based on the full-analysis set (FAS), consisting of all patients who took at least 1 dose of study medication and who had at least 1 valid postbaseline YBOCS assessment. The relationship between demographic parameters (age, sex) and baseline symptom severity was assessed in the pooled population of patients from both studies.

Analysis of Symptomatic Response on Disability and HRQoL

To assess the relationship between baseline symptom severity and impairment in functioning or HRQoL, data from the FAS were pooled for both studies. Baseline impairment in HRQoL was assessed by standardizing the scores for each SF-36 dimension using population mean and standard deviations derived from published US normative data[32] (standard scores were calculated as *z* scores [mean score for each SF-36 dimension = population mean/population standard deviation]). The relationship between baseline severity and impaired function or HRQoL was assessed by grouping patients into those with more severe or less severe symptoms. Grouping was based on a median split of the baseline YBOCS score from the fixed-dose study, as specified a priori in the protocol for that study. Patients with a baseline YBOCS ≥ median were characterized as having more severe symptoms and those with a baseline YBOCS < median were characterized as less severe. Between-group differences were analyzed using Student *t* test ($\alpha = .05$).

The comparative effects of escitalopram, paroxetine, and placebo on SDS and SF-36 scores were analyzed from the fixed-dose study using an analysis of covariance, with treatment and center as factors, and baseline SDS or SF-36 score as a covariate (FAS, last observation carried forward).

To assess the relationship between YBOCS-defined categorical outcomes and functional or HRQoL outcomes, analyses (Student *t* test or Wilcoxon, when relevant, according to the normality and homoscedasticity of the data) were conducted for responders versus nonresponders (fixed-dose study) or for relapsed versus nonrelapsed patients (relapse-prevention study). Pearson correlations were performed on the pooled FAS dataset to analyze the relationship between symptomatic severity, disability, and HRQoL.

Medical Outcomes Study Short Form scores were transformed into utility values using the SF-6D algorithm.[33] Utility is an index value of HRQoL ranging from 0 (death) to 1 (perfect health) that can be used for further calculation of cost-effectiveness and quality-adjusted life-years. Utilities were calculated at baseline and for the health states of response and relapse.

Table 1. Baseline SF-36 Scores in Comparison to Published US Norms (FAS, pooled data)

SF-36 Dimension	Baseline	US Norm[32]	*z* Score[a]
PF	84.1 ± 20.8	84.2 ± 23.3	−0.14
RP	62.1 ± 41.1	81.0 ± 34.0	−0.64
BP	70.1 ± 26.9	75.2 ± 23.7	−0.23
GH	55.2 ± 22.5	72.0 ± 20.3	−0.74
SF	46.1 ± 25.8	83.3 ± 22.7	−1.67
MH	47.2 ± 19.0	51.7 ± 18.4	−1.62
RE	37.5 ± 38.4	81.3 ± 33.0	−1.45
VT	42.3 ± 18.9	60.9 ± 21.0	−0.95

[a]Mean score for each SF-36 dimension = population mean/population standard deviation.

Abbreviations: BP = bodily pain, FAS = full-analysis set, GH = general health perceptions, MH = mental health, PF = physical functioning, RE = role limitations due to emotional problems, RP = role limitations due to physical health problems, SF = social functioning, SF-36 = Medical Outcomes Study Short Form, VT = vitality.

RESULTS

Study Population

In the fixed-dose study,[24] 466 patients with a mean age at onset of OCD of 23 years with a mean duration since onset of 14 years received study medication. The patients had moderate-to-severe OCD (mean YBOCS = 27) and were randomized 1:1:1:1 to 24-week treatment with placebo, paroxetine 40 mg, escitalopram 10 mg, or escitalopram 20 mg. The FAS consisted of 455 patients.

In the relapse-prevention study, there were 468 patients who initiated open-label treatment with escitalopram and 466 in the FAS.[25] These patients suffered from moderate-to-severe OCD (mean YBOCS score of 26.4), with a mean age at onset of OCD of approximately 23 years and mean duration since onset similar of 13–14 years.

Baseline Disability and HRQoL

The baseline SDS and SF-36 scores were calculated for the FAS pooled from both studies (N = 921 patients). Baseline scores on the SDS subscales for family life, social life, and work were 6.2, 6.3, and 6.3, respectively. Baseline SF-36 scores are reported in Table 1. For comparison purposes, baseline SF-36 scores are plotted along with norms from a US population[32] and scores for OCD patients reported in 2 previous publications[6,8] in Figure 1. The mean SF-36 scores on the 4 mental health domains (vitality, social functioning, role limitations due to emotional problems, and mental health) were at least 1 *z* score unit lower than the US norm.

Baseline SDS and SF-36 scores were analyzed as a function of baseline symptom severity, with patients scoring above the median YBOCS score of 26.5 being categorized as having more severe symptoms and those scoring below being categorized as having less severe symptoms. Half of the patients (461, 50%) were categorized as suffering from more severe symptoms (YBOCS ≥ 27). Compared to those with

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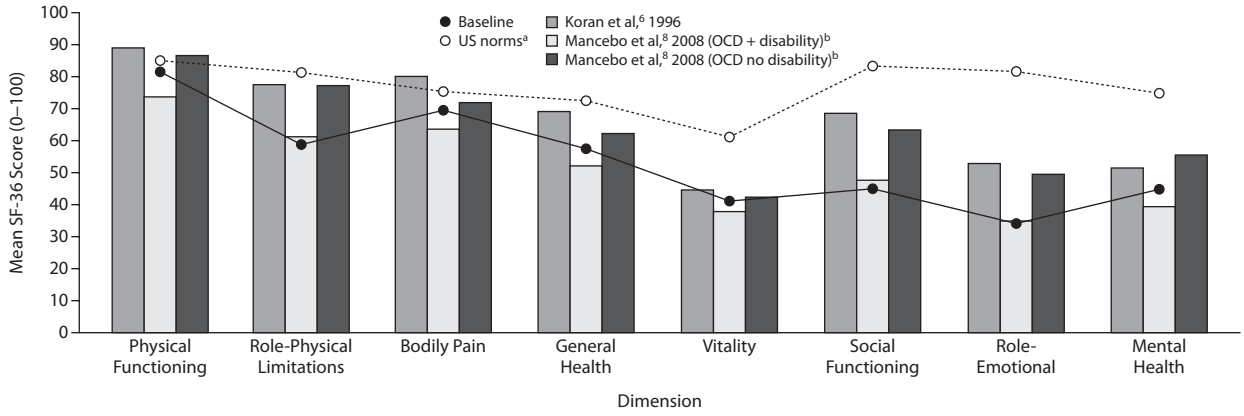
Figure 1. Mean Baseline SF-36 Scores for Each of the 8 Dimensions (pooled FAS, n = 921) in Comparison to Published US Norms and Baseline Data From 2 Published Studies of Impact of OCD on SF-36 Scores



[a]Data from Ware et al,[32] 1993.
[b]Mancebo et al[8] reported SF-36 scores for OCD patients with occupational disability (OCD + disability) or without occupational disability (OCD no disability). Occupational disability was confirmed by asking patients if they were receiving disability payments due to OCD at the time of the interview.
Abbreviations: FAS = full-analysis set, OCD = obsessive-compulsive disorder, SF-36 = Medical Outcomes Study Short Form.

Table 2. Relationship Between Baseline SDS and SF-36 Scores and Baseline Severity Defined by YBOCS Score (FAS, pooled data, n = 921)[a]

	Less Severe (YBOCS ≤ 26)	More Severe (YBOCS ≥ 27)	Difference	*P* Value
SDS				
Family life	5.3 ± 2.4	7.1 ± 2.2	−1.8	.001
Social life	5.4 ± 2.4	7.1 ± 2.2	−1.7	.001
Work	5.3 ± 2.3	7.2 ± 1.8	−1.9	.001
SF-36				
PF	86.9 ± 17.5	81.3 ± 23.3	5.6	.008
RP	67.9 ± 38.2	56.3 ± 43.1	11.6	.001
BP	71.1 ± 25.6	69.1 ± 28.2	2.0	.53
GH	61.0 ± 20.9	49.4 ± 22.6	11.6	.001
SF	53.4 ± 24.8	38.7 ± 24.7	14.7	.001
MH	51.3 ± 18.9	43.0 ± 18.1	8.3	.001
RE	45.3 ± 39.1	29.6 ± 35.9	15.7	.001
VT	45.5 ± 19.2	39.0 ± 18	6.5	.001

[a]Between-group differences were analyzed using Student *t* test.
Abbreviations: BP = bodily pain, FAS = full-analysis set, GH = general health perceptions, MH = mental health, PF = physical functioning, RE = role limitations due to emotional problems, RP = role limitations due to physical health problems, SDS = Sheehan Disability Scale, SF = social functioning, SF-36 = Medical Outcomes Study Short Form, VT = vitality, YBOCS = Yale-Brown Obsessive Compulsive Scale.

Table 3. Sheehan Disability Scale Subscale Scores (fixed-dose study, n = 455; FAS, LOCF)

	Baseline, Mean ± SD	Difference ± SE From Baseline		
		Week 6	Week 12	Week 24
Work				
PBO	6.4 ± 2.4	−1.31 ± 0.27	−1.85 ± 0.29	−1.79 ± 0.32
ESC10	6.3 ± 2.0	−1.40 ± 0.25	−2.41 ± 0.27	−2.99 ± 0.30**
ESC20	6.2 ± 2.2	−2.08 ± 0.26*	−2.76 ± 0.28*	−2.69 ± 0.30*
PAR40	6.3 ± 2.5	−1.78 ± 0.25	−2.46 ± 0.28	−2.82 ± 0.31*
Social life				
PBO	6.6 ± 2.5	−1.49 ± 0.24	−1.27 ± 0.25	−1.60 ± 0.29
ESC10	6.3 ± 2.1	−1.55 ± 0.24	−2.47 ± 0.24***	−2.92 ± 0.28***
ESC20	6.1 ± 2.1	−1.87 ± 0.24	−2.53 ± 0.24***	−2.69 ± 0.27**
PAR40	6.4 ± 2.2	−2.09 ± 0.24	−2.66 ± 0.24***	−2.90 ± 0.28***
Family life				
PBO	6.4 ± 2.5	−1.46 ± 0.25	−1.44 ± 0.26	−1.74 ± 0.29
ESC10	6.5 ± 2.2	−1.69 ± 0.25	−2.59 ± 0.25**	−3.12 ± 0.28***
ESC20	6.3 ± 2.4	−1.91 ± 0.25	−2.29 ± 0.25*	−2.68 ± 0.27*
PAR40	6.5 ± 2.5	−1.93 ± 0.25	−2.63 ± 0.26**	−2.98 ± 0.28**

*$P < .05$, **$P < .01$, ***$P < .001$ versus placebo based on ANCOVA.
Abbreviations: ANCOVA = analysis of covariance, ESC10 = escitalopram 10 mg/d, ESC20 = escitalopram 20 mg/d, FAS = full-analysis set, LOCF = last observation carried forward, PAR40 = paroxetine 40 mg/d, PBO = placebo.

a YBOCS score ≤ 26 at baseline, the more severe patients reported statistically significantly greater impairment on all dimensions of the SF-36 except bodily pain and statistically significantly greater disability scores on each of the 3 SDS subscales (Table 2).

Impact of Treatment on Disability and HRQoL: Fixed-Dose Study

Sheehan Disability Scale. Table 3 summarizes the effects of each treatment on the 3 subscales of the SDS in the randomized study; the mean SDS subscale scores for work, social life, and family life decreased from approximately 6 (moderately impaired) at baseline to approximately 3 (mildly impaired) for the active treatment groups. At the 12-week primary efficacy endpoint, all active treatment groups showed a statistically significant improvement compared to placebo on the social life and family life subscales. By week 24, there were statistically significant improvements in all 3 subscales. For the work subscale, only escitalopram 20 mg showed a significant improvement at weeks 6 and 12.

SF-36. The effects of escitalopram, paroxetine, and placebo on each of the SF-36 dimensions are shown in Figure 2 (after 12 weeks of treatment) and Figure 3 (after 24 weeks of treatment). Statistically significant improvements (vs placebo) were seen for patients receiving escitalopram or paroxetine on each of the 4 mental health domains (vitality, social functioning, role-emotional, and mental health) at the 12-week primary endpoint. These improvements were sustained or improved through to the end of 24 weeks.

The effects of escitalopram and paroxetine on the physical health dimensions were less pronounced, although improvements in general health (vs placebo) were evident as early as

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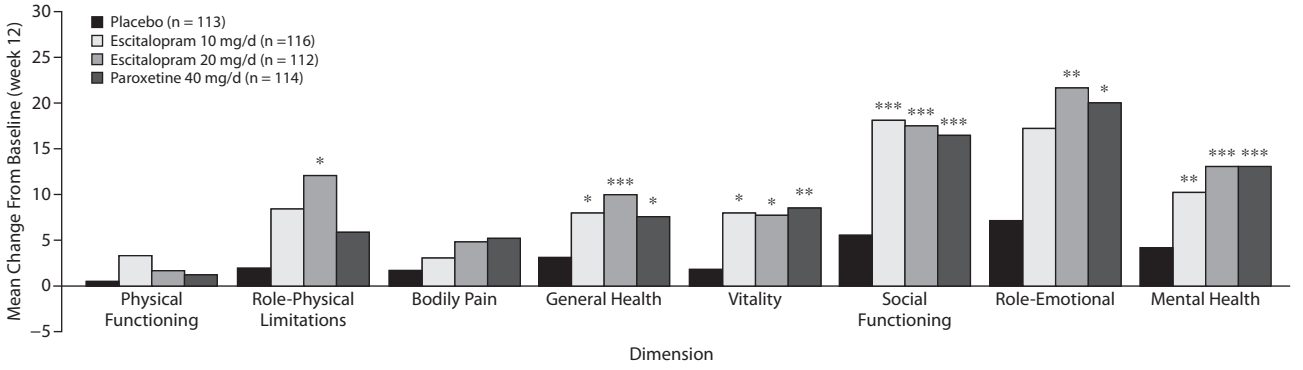
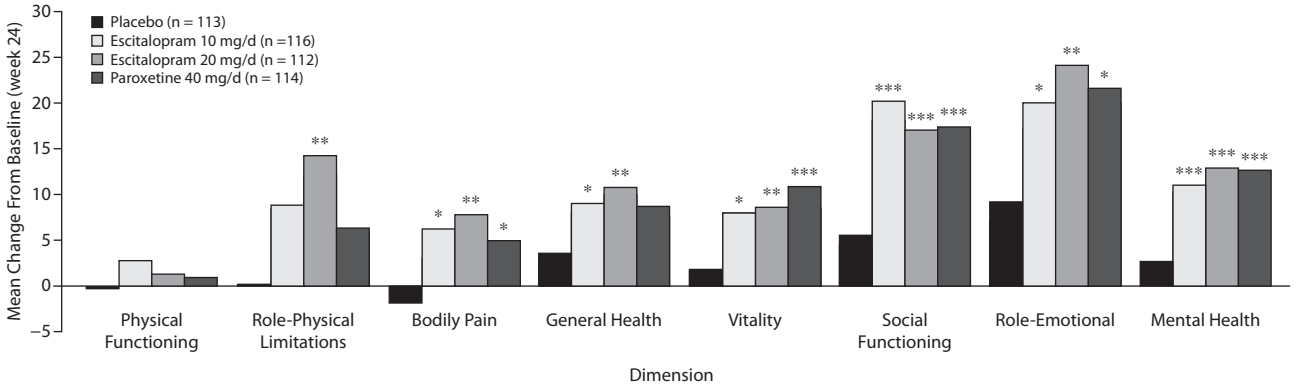
Figure 2. Mean Change in SF-36 Score From Baseline to the End of 12 Weeks (primary endpoint) in Patients Receiving Fixed-Dose Treatment With Escitalopram, Paroxetine, or Placebo (fixed-dose study[24]; FAS, LOCF)



*$P < .05$, **$P < .01$, ***$P < .001$ versus placebo (ANCOVA).
Abbreviations: ANCOVA = analysis of covariance, FAS = full-analysis set, LOCF = last observation carried forward, SF-36 = Medical Outcomes Study Short Form.

Figure 3. Mean Change in SF-36 Score From Baseline to the End of 24 Weeks in Patients Receiving Fixed-Dose Treatment With Escitalopram, Paroxetine, or Placebo (fixed-dose study[24]; FAS, LOCF)



*$P < .05$, **$P < .01$, ***$P < .001$ versus placebo (ANCOVA).
Abbreviations: ANCOVA = analysis of covariance, FAS = full-analysis set, LOCF = last observation carried forward, SF-36 = Medical Outcomes Study Short Form.

week 12. However, improvements on the bodily pain dimension did not reach statistical significance until week 24. The mean change from baseline on the role-physical dimension was statistically significantly different from placebo only for patients receiving 20 mg/d of escitalopram. This difference was apparent at week 12 and was sustained until week 24.

Impact of Symptomatic Response on Disability and Quality of Life

Fixed-dose study. Among the 455 patients in the FAS from the fixed-dose study, 342 received active treatment. Of these, 224 (65.4%) had responded to treatment after 12 weeks (primary endpoint). Compared to nonresponders, responders reported significantly less disability on each of the SDS subscales (Table 4). Similarly, responders had an overall higher HRQoL with statistically significantly greater scores on all SF-36 dimensions (except for bodily pain) and significantly higher utility (Table 5).

At endpoint, there was a significant correlation between YBOCS score (compulsive and obsessive dimensions) and SDS total score ($r = 0.7$, $P < .001$). There were also significant correlations between YBOCS score and each SF-36 dimension score at the 12-week endpoint (Pearson correlation, $P < .001$). The correlation was greatest for the 4 mental health dimensions, each with the Pearson correlation coefficient ≥ 0.5. The Pearson correlation coefficients for the 4 physical health domains were all ≤ 0.4 (data not shown).

Relapse-prevention study. The impact of relapse on SDS and SF-36 scores was assessed in 320 patients who responded to open-label, flexible-dose treatment with escitalopram and who were then randomized to receive double-blind treatment with escitalopram or placebo. Sheehan Disability Scale subscores and SF-36 dimension scores at randomization were not predictive of future relapse (data not shown). At endpoint, 119 patients had relapsed (81 from the placebo group and 38 from the escitalopram group). Relapsed patients reported significantly greater functional impairment on all 3 SDS subscales. The mean subscale scores at the last assessment for relapsed and nonrelapsed patients (respectively) were family life: 4.59 versus 2.05; social life: 4.39 versus 1.96;

Table 4. Disability and HRQoL Scores in Patients Achieving Response (≥ improvement in YBOCS at week 24) or No Response to Treatment (fixed-dose study, n = 342; FAS, LOCF)[a]

	Active Treatment			
	Nonresponders (n = 118)	Responders (n = 224)	Difference	*P* Value
SDS				
Family life	5.8 ± 2.5	2.8 ± 2.3	3.0	< .001
Social life	5.8 ± 2.4	2.6 ± 2.0	3.2	< .001
Work	5.7 ± 2.4	2.7 ± 2.1	3.0	< .001
SF-36				
PF	84.3 ± 20.4	91.5 ± 15.2	−7.2	< .001
RP	65.5 ± 41.3	79.6 ± 33.8	−14.2	.003
BP	72.2 ± 25.1	76.9 ± 23.5	−4.7	.10
GH	54.5 ± 21.8	64.8 ± 19.3	−10.3	< .001
SF	52.4 ± 26.6	72.5 ± 21.6	−20.1	< .001
MH	52.6 ± 19.5	66.6 ± 16.6	−14.0	< .001
RE	47.9 ± 39.4	68.0 ± 38.6	−20.1	< .001
VT	43.4 ± 20.1	56.6 ± 19.0	−13.3	< .001

[a]Between-group differences were analyzed using Student *t* test.
Abbreviations: BP = bodily pain, FAS = full-analysis set, GH = general health perceptions, HRQoL = health-related quality of life, LOCF = last observation carried forward, MH = mental health, PF = physical functioning, RE = role limitations due to emotional problems, RP = role limitations due to physical health problems, SDS = Sheehan Disability Scale, SF = social functioning, SF-36 = Medical Outcomes Study Short Form, VT = vitality, YBOCS = Yale-Brown Obsessive Compulsive Scale.

and work: 4.50 versus 1.77 (all $P < .01$). Likewise, relapsed patients had significantly lower scores on all 8 dimensions of the SF-36 compared to nonrelapsed patients (Figure 4) (data not shown).

At last assessment, nonrelapsed patients receiving escitalopram reported significantly less disability on the family life and work subscales of the SDS ($P < .05$) and significantly better scores on the SF-36 dimensions for social functioning, mental health, and role-emotional limitations ($P < .01$) compared to those receiving placebo. Health utility was significantly higher for nonrelapsed compared to relapsed patients (Table 5).

During the open-label period of the relapse-prevention study treatment, most patients (386 of 468 patients) who received escitalopram 20 mg/d had decreased SDS subscale scores from baseline to week 8 and from week 8 to week 16. Compared to nonresponders, those who achieved response by the end of the 16-week open-label period reported significantly higher scores on all SF-36 dimensions except for bodily pain.

DISCUSSION

Collectively, analyses of the data from the fixed-dose and relapse-prevention trials provide evidence that the SDS and SF-36 are sensitive to baseline symptom severity (as measured by the YBOCS), to symptom improvement (YBOCS-defined responders), and to symptom deterioration (YBOCS-defined relapses). When patients with OCD were stratified on the basis of baseline symptom severity defined by YBOCS scores, they were also distinguished by statistically significant differences in SDS and SF-36 scores.

The analyses of baseline SDS and SF-36 data pooled from over 900 patients participating in both trials revealed

Table 5. Utility Values Based on SF-36 Scores (n = 455)[a]

	Mean Utility Value (± SD)
Baseline value	0.648 ± 0.103
Response	0.725 ± 0.108
No response	0.664 ± 0.106***
Relapse	0.684 ± 0.116
No relapse	0.776 ± 0.113***

[a]Between-group differences (response vs nonresponse, relapse vs nonrelapse) were analyzed using Student *t* test.
***$P < .001$.
Abbreviation: SF-36 = Medical Outcomes Study Short Form.

considerable disability among patients with OCD. The degree and pattern of baseline impairment on the SF-36 is comparable to reports from studies of generalized anxiety disorders[34–36] and to previously published reports involving smaller samples of OCD patients with a similar degree of symptom severity (see Figure 1). For instance, Koran[37] collected SF-36 scores from 60 OCD patients (mean YBOCS score of 26.8) and reported similar impairment. More recently, Mancebo and colleagues[8] assessed over 200 consecutive OCD patients with or without occupational disability (defined as patients who were not working due to psychopathology). Patients with occupational disability had SF-36 scores similar to patients included in the present analyses.

It has been proposed that a between-group difference of 10 points on any SF-36 domain represents a reasonable threshold for interpreting clinical relevance.[33] To apply this criterion to the present data, the differences between patients with OCD and US norms were clinically relevant on each of the 4 mental health domains, as well as domains for general health and role-physical. Evidence supporting the clinical relevance of these differences comes from the *z* score analyses. On their own, the generation of *z* scores based on data from previously published norms may lack validity; however, the results do correspond with the SF-36 differences scores. On each of the SF-36 mental health dimensions, OCD patients were at least 1 *z* score unit below the published US population norms. The differences were less pronounced on the physical health domains, but the dimensions for general health and role limitations due to physical problems (role-physical) were each more than half a *z* score unit below the norm, also suggesting a relevant level of impairment.

At present, there is no consensus on a YBOCS cut-off score that defines severe OCD. In the present analyses, a median split was predefined to categorize patients into those with relatively more or relatively less severe symptoms. Those patients with more severe symptoms (YBOCS score ≥ 27) had statistically significantly greater levels of impairment on the 3 SDS subscales and each of the SF-36 dimensions except bodily pain. The results of this analysis, along with comparability in the SF-36 scores between the present patients and the OCD patients with occupational disability studied by Mancebo and colleagues[8] (mean YBOCS score of 26.5), suggest that a YBOCS cut-off score of 26–27 represents a clinically relevant degree of functional disability, not only on mental health domains but also in general health and the performance of occupational roles and functions.

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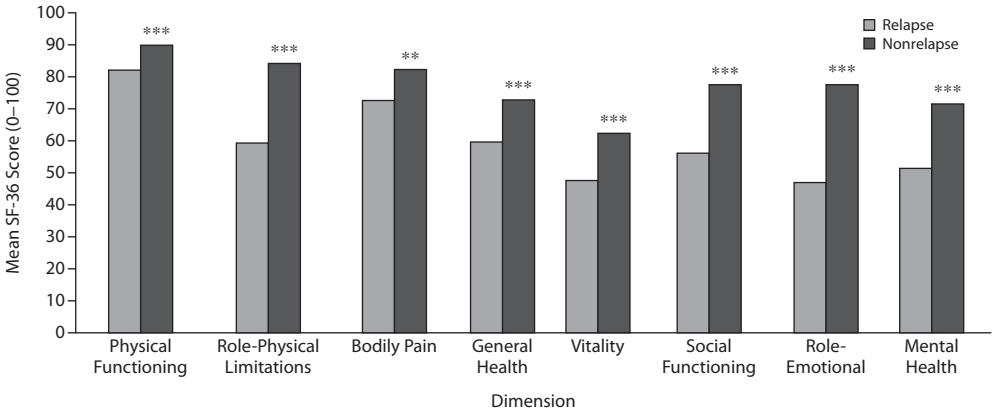
Figure 4. Mean SF-36 Scores at Last Assessment for Relapsed (n = 119) and Nonrelapsed (n = 201) Patients (relapse-prevention study[25])



*P < .05, **P < .01, ***P < .001 versus placebo (ANCOVA).
Abbreviations: ANCOVA = analysis of covariance, SF-36 = Medical Outcomes Study Short Form.

Although preliminary in nature, these results do suggest that a threshold of symptom severity, measurable using the YBOCS, might identify patients with clinically relevant disability. Identifying a corresponding cut-off score on the YBOCS may have clinical utility and thus provides grounds for further research in this area.

There is limited evidence that pharmacologic treatment of OCD improves long-term functioning and HRQoL. We are aware of only 1 published pharmacotherapy trial that was sufficiently powered to show efficacy and included a functional assessment (SDS). In that 12-week study, citalopram was shown to improve OCD symptoms and SDS ratings compared to placebo.[30] The present analyses show functional improvements compared to placebo on the SDS and SF-36 over a 24-week period. Using the criterion of a 10-point difference from baseline, clinically relevant improvements on the SF-36 were reported on all 4 mental health domains after 12 weeks of treatment with escitalopram 20 mg/d and paroxetine 40 mg/d. Only patients receiving 20 mg of escitalopram reported clinically relevant improvements in general health (after both 12 and 24 weeks) and in role limitations due to physical problems (after 12 and 24 weeks).

Monitoring patients over an extended period may be particularly important for assessing outcomes related to work functioning, for which peak improvements may be achieved over a longer period of time than is required to see statistically significant symptom improvements, and disabilities may persist despite significant symptom reduction, as previously reported in patients with depression.[17,18] Indeed, the analyses of the SDS work subscale and the SF-36 role-limitations dimensions seem to indicate that, overall, improvements in these measures are relatively more difficult to achieve than improvements on the other social or mental health dimensions. For instance, on the SDS, work function improved progressively with each antidepressant group reporting statistically significantly higher scores compared to placebo after 24 weeks. However, at early assessments (6 and 12 weeks), only patients receiving the high dose of escitalopram achieved statistically significant improvements compared to placebo. Similarly, on the SF-36, only patients receiving the high dose of escitalopram reported statistically significant and clinically relevant improvements on the role-physical dimension. It is not clear why escitalopram-treated patients reported statistically significantly better scores on some work-related assessments. These results may hint at subtle efficacy advantages or better tolerability, which have been observed in previous studies involving depressed and anxious patients.[38–40] Nevertheless, these differences should be interpreted with caution as the primary efficacy and tolerability analyses in the fixed-dose study did not yield statistically significant differences between medications.

Although there is some consensus regarding the definition of categorical outcomes, such as response and relapse in OCD,[38] there remains considerable variability between trials. Treatment response is commonly defined as a 25%–35% reduction from baseline on the YBOCS score,[38] whereas definitions of relapse vary considerably from one trial to the next.[25,39,40] An important step toward achieving a consensus for any given outcome based on a YBOCS criterion is to demonstrate that such a criterion distinguishes patients on the basis of a clinically meaningful assessment that varies as a function of YBOCS score. Pallanti and colleagues[38] have suggested that HRQoL can be a crucial tool for evaluating response to treatment. Concordant with this suggestion, in the present analyses, improvements on the SDS and SF-36 were closely correlated with improvements in YBOCS score. When response was defined using the YBOCS criterion of at least a 25% improvement in total score relative to baseline, the mean SDS and SF-36 scores for responders and nonresponders were clearly distinguishable; there were statistically significant and clinically relevant differences (at least 10-point difference) on each of the 4 mental health subscales as well as on general health and the role-physical dimension. Thus, with respect to mental health and work-related functional outcomes, it seems that a 25% improvement in YBOCS score, while not the ultimate

goal of treatment, nonetheless represents a clinically relevant achievement and is concordant with the consensus[38] that this level of improvement represents at least a partial response in OCD.

Complementary to concomitant improvements in symptoms and function, the present analyses also reveal, for the first time, a relationship between symptom deterioration (relapse) and functional impairment. Compared with patients who achieved and maintained response, patients who relapsed reported statistically significantly worse outcomes on the SDS and SF-36. Difference scores on each of the SDS dimensions were approximately 2.5 points, and mean scores represent the difference between patients reporting moderate (relapsed patients) compared to mild disability. For the SF-36, the between-group differences were clinically relevant, exceeding 10 points for all of the SF-36 dimensions except for physical functioning.

The relationship between symptomatic improvement, function, and HRQoL reported here is consistent with some previous studies assessing treatment efficacy in OCD patients.[12,28,30] However, these results are in contrast to other studies in which substantial disability and HRQoL impairments were reported to persist despite, or were unrelated to, symptomatic improvement.[5,11,16] There is no obvious explanation for the inconsistent results between studies. In the majority of these studies, subjects were outpatients with a baseline symptom severity around 26 points on the YBOCS. Although it is difficult to validly compare outcomes between studies, where the data are available, the magnitude of improvement on the YBOCS was comparable. Thus, neither baseline severity nor posttreatment efficacy seems to easily account for differences between studies. An alternate explanation may be that some HRQoL measures are simply not sensitive to change in OCD patients.

The limitations of each of the studies reported in this article have been discussed at length elsewhere;[24,25] however, there are limitations unique to the present analysis that warrant consideration. First, it should be noted that patients included in these studies were required to score at least 20 on the YBOCS at baseline. By requiring a minimum level of symptom severity, it may be that patients were inadvertently selected to have a minimum level of disability. Thus, the baseline level of disability and HRQoL impairment seen in this sample of patients may not reflect that of the general population of OCD patients. With this in mind, it is also relevant that these trials were designed to evaluate the clinical efficacy of escitalopram in OCD patients who were not experiencing significant comorbid depression, other anxiety symptoms, or other *DSM* Axis I disorders. Consequently, the level of baseline impairment and the relationship between symptom severity and disability or HRQoL observed here may not generalize to patients with more complex disorders. Furthermore, patients in these studies were generally middle aged and were enrolled mostly from secondary or tertiary care centers, and it is possible, therefore, that these patients may suffer from more refractory OCD than younger patients seen in primary care.

CONCLUSION

To our knowledge, these are the first data from large, long-term, well-controlled trials to evaluate disability and HRQoL outcomes in OCD patients as a function of symptom improvement or deterioration. The results from the fixed-dose and relapse-prevention trials provide clear evidence for a relationship between symptom severity and functional impairment in OCD patients. There were statistically significant and clinically relevant differences between patients with more severe symptoms compared to those with less severe symptoms. Furthermore, there is complementary and congruent evidence that (1) long-term pharmacologic treatment of OCD with escitalopram or paroxetine improves function and quality of life (although escitalopram may have a preferential benefit in work-related function) and (2) that symptom relapse is associated with deterioration in function and quality of life. Not only were between-group differences (ie, responders vs nonresponders; relapse vs nonrelapse) statistically significant, but the available evidence suggests that in terms of mental health and role functioning, the differences were also clinically relevant. The present analyses further provide evidence that the SDS and SF-36 are sensitive to treatment outcomes in OCD and provide support for YBOCS cut-off scores that are commonly used to define treatment outcomes.

Drug names: clomipramine (Anafranil and others), escitalopram (Lexapro and others), paroxetine (Paxil, Paxeva, and others).

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