Posttraumatic Stress Disorder and Quality of Life: Results Across 64 Weeks of Sertraline Treatment

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Objective: The goal of the current study was to characterize the quality of life (QOL) and functional impairment associated with posttraumatic stress disorder (PTSD) and to report the QOL/functional response over the course of long-term treatment.

Method: QOL and psychosocial functioning were analyzed in 359 randomly assigned patients across a 3-phase study of sertraline in the treatment of chronic DSM-III-R–defined PTSD: (1) 12 weeks of double-blind, placebo-controlled *acute* treatment with sertraline in flexible doses of 50 to 200 mg/day, (2) 24 weeks of open-label *continuation* treatment with sertraline among all study completers (regardless of initial study drug assignment or endpoint responder status), and (3) 28 weeks of double-blind, placebo-controlled *maintenance* treatment with sertraline in continuation phase responders. Assessments included the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q), emotional role functioning and mental health subscales of the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36), as well as the occupational and social functioning items on the Clinician-Administered PTSD Scale, Part 2 (CAPS-2).

Results: At acute phase baseline, QOL was significantly impaired as reflected by a mean Q-LES-Q score of 56% of the total possible score and a CAPS-2 social/occupational impairment composite score of 4.4. Sertraline treatment was associated with marked improvement on all QOL/functional measurements: at the end of the acute treatment phase, 58% of responders on treatment with sertraline had achieved Q-LES-Q total scores within 10% of community norms. Twenty-four weeks of continuation treatment led to an additional 20% improvement in QOL and measures of functioning. Double-blind discontinuation of sertraline resulted in recurrence of PTSD symptoms and a worsening of QOL and functional measures, although the degree of exacerbation in symptomatology and psychosocial impairment was notably less than at study entry.

Conclusion: Sertraline treatment of chronic PTSD is associated with rapid improvement in quality of life that is progressive and sustained over the course of more than 1 year of treatment.

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Traditionally, treatment efficacy has been evaluated by assessing change in target symptoms of the illness, while quality of life (QOL) and functional outcomes have been ignored. Yet QOL, functioning, and symptomatology appear to be largely orthogonal outcome domains. In fact, QOL improvement has been shown to differ among treatment responders who experienced equivalent improvement on traditional symptom measures.[1] Despite an increasing recognition of the importance of QOL/functional status as clinical outcomes, little is known about either the baseline clinical determinants of QOL/functional impairment or the time course of improvement in QOL/functioning with long-term treatment.

Depressive and anxiety disorders have been shown to have a significantly negative impact on an individual's perceived ability to enjoy life and function normally.[2] The mean Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q)[3] score has been reported to be 42% in hospitalized psychiatric patients,[4] 53% in patients suffering from chronic major depression,[5] 60% in obsessive-compulsive disorder,[6] and 67% in panic disorder.[1]

Posttraumatic stress disorder (PTSD) is notable among anxiety disorders for its chronicity,[7,8] high degree of comorbidity and associated disability, impaired quality of life, and health-related problems.[9–15] However, recent PTSD research suggests that a variety of treatment modalities are efficacious in the acute treatment of PTSD including cognitive-behavioral therapies[16–21] and antidepressants such as tricyclics,[22,23] monoamine oxidase inhibitors,[21] and selective serotonin reuptake inhibitors (SSRIs).[24–30] The efficacy of sertraline has been demonstrated for the acute treatment of PTSD,[29] as well as during continuation[31] and maintenance therapy.[32]

The current article reports the functional and QOL outcomes for acute, continuation, and maintenance studies of sertraline.[29–32] The purpose of the current report is to assess the effect of sertraline treatment on QOL and perceived functioning across acute, continuation, and double-blind maintenance phases of treatment and to evaluate correlates of baseline QOL/functional impairment associated with chronic PTSD. We hypothesized (1) that treatment with sertraline would enhance QOL and improve measures of functioning, (2) that continuation treatment with sertraline would result in further consolidation of improvements in QOL/functioning, and (3) that discontinuation of sertraline during what could be conceptualized as the maintenance phase of treatment would be associated with a significant decrement in QOL and functioning.

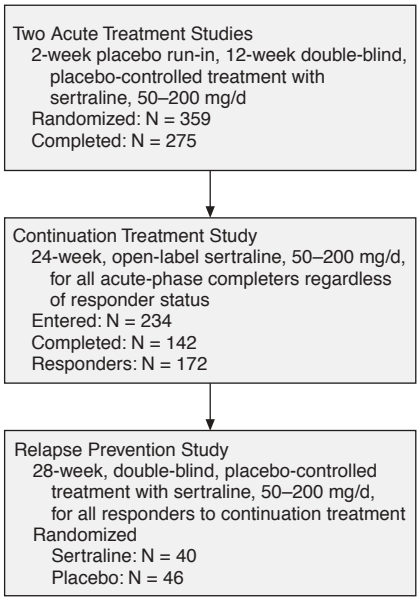
METHOD

After a complete description of the study was provided to the patients, written informed consent was obtained prior to the start of acute study treatment. Written informed consent was obtained from patients entering the acute treatment trials, again at entry into the continuation trial, and again at the baseline of the maintenance treatment study.

Figure 1 presents a schematic overview of the 3 phases of study treatment that form the basis for the current report. The entry criteria and design for each study phase are presented in detail in the initial reports.[30–32] Briefly, male and female outpatients were randomly assigned to 1 of 2 identical acute, placebo-controlled, sertraline treatment studies if they were 18 years of age or older and met criteria for a principal diagnosis of PTSD as determined by the Structured Clinical Interview for DSM-III-R (SCID)[33] of at least 6 months' duration and had a baseline Clinician-Administered PTSD Scale, Part 2 (CAPS-2)[34] total severity score ≥ 50. Female patients were excluded from study participation if they were pregnant or lactating, or fertile and not using a medically accepted form of contraception. Patients were also excluded if they had a current or past history of bipolar or psychotic disorder, organic mental disorder, factitious or malingering disorder; had a primary diagnosis of major depression, obsessive-compulsive disorder, or other anxiety disorder; or met criteria for alcohol or substance dependence or abuse in the past 6 months.

Patients who completed the acute phase of treatment, whether or not they were responders, were permitted to enter the 24-week continuation phase, in which treatment consisted of open-label sertraline in flexible daily doses ranging from 50 to 200 mg/day. All patients who completed continuation treatment as responders (defined as a Clinical Global Impressions-Improvement [CGI-I] score ≤ 2 and ≥ 30% reduction in CAPS-2 total score) and provided renewed consent were randomly assigned, in a double-blind manner, to continue sertraline or to receive placebo for 28 additional weeks in a relapse prevention study.

Figure 1. Patient Flow Diagram



Outcome Measures

The following measures were used to evaluate the effect of treatment on patient QOL and functional status:

1. The short form of the patient-rated Q-LES-Q[3] was used to assess an individual's perceived quality of life and satisfaction across multiple domains. The short form of the Q-LES-Q consists of 16 items rated by the patient on a 5-point Likert scale. The first 14 items are summed to produce a total QOL score whose maximum is 70 (or 100% of the possible maximum score). In addition, 2 global items are scored individually. The scale is scored as a percent of the total possible score.
2. Two of the 8 subscales (emotional role functioning and mental health) of the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36)[35] were used to measure the impact of PTSD on psychological functioning and well-being.
3. The occupational impairment and social impairment items of the CAPS-2 were used as a disease-specific measure of dysfunction.[36,37] These items were rated on a 5-point severity scale, and a composite CAPS-2 impairment score was created by summing the score for each individual item.

The primary efficacy measures used throughout all 3 study phases were the CAPS-2, which provides a 17-item total severity score; the Impact of Event Scale,[38] the original 15-item patient-rated scale, which differs from the current revised version in not including the DSM-IV core

Table 1. Demographic and Clinical Variables of 359 Patients at Acute Phase Sertraline Treatment of Chronic DSM-III-R PTSD at Baseline[a]

Variable	Value
Female, %	73.3
Age, mean ± SD, y	38.3 ± 10.6
Race, %	
Black	9.7
White	86.9
Other	3.4
Duration of illness, mean ± SD, y[b]	11.4 ± 11.6
History of childhood trauma, %	10.5
Baseline 17-item CAPS-2 score, mean ± SD	74.0 ± 16.6
Baseline HAM-D (17-item) total score, mean ± SD	21.1 ± 7.5
Baseline Q-LES-Q score, mean ± SD	55.7 ± 12.0
Baseline CAPS-2 social/occupational impairment composite score, mean ± SD	4.4 ± 1.4
Presence of comorbid major depression	43.2
Time from traumatic event, mean ± SD, y[b]	17.1 ± 14.0
Frequency of trauma by category, %	
Serious accident, injury, or fire	8.8
Physical or sexual assault	59.1
Seeing someone hurt or die	12.8
Being in war or combat	5.1
Miscellaneous other events	14.2

[a]Abbreviations: CAPS-2 = Clinician-Administered Posttraumatic Stress Disorder Scale, Part 2; HAM-D = Hamilton Rating Scale for Depression; PTSD = posttraumatic stress disorder; Q-LES-Q = Quality of Life Enjoyment and Satisfaction Questionnaire.
[b]The *time from traumatic event* is a retrospective measure of the time when the most significant trauma occurred, while *duration of illness* reflects a retrospective assessment when patients met full criteria for PTSD.

cluster of hyperarousal (data on this scale are included in the primary reports, but are not included in the present study); and the Clinical Global Impressions-Severity of Illness (CGI-S) and CGI-I.[39] Results for these primary efficacy measures in this patient population are reported in previous articles.[29–32]

Statistical Analyses

Means and standard deviations were computed for the 2 acute-phase studies at baseline for age, duration of illness, time from traumatic event, 17-item CAPS-2 score, 24-item Hamilton Rating Scale for Depression[40] total score, Q-LES-Q score, and CAPS-2 social/occupational impairment composite score. In addition, the proportions of women, white patients, patients with a history of childhood trauma, patients in each marital status category, patients with comorbid depressive disorder, and the proportion of patients within each type of trauma category were computed.

Change from baseline in Q-LES-Q total score and CAPS-2 social/occupational impairment composite score at the end of the acute-phase study, and after 28 weeks of double-blind maintenance treatment, were analyzed using an analysis of covariance (ANCOVA) model with terms for baseline, treatment, and protocol in the model. The analysis was performed for intent-to-treat patients using their last observation carried forward (LOCF) and for patients who completed the study using their week 12 or week 28 observed value. The SF-36 emotional role functioning and mental health domains were analyzed for the subgroup of patients with and without depressive comorbidity; an ANCOVA was used to compare the 2 treatment groups for each of the 2 subgroups. Means and standard deviations for Q-LES-Q, CAPS-2 social/occupational impairment composite score, and SF-36 were computed for the 3 treatment phases for the subgroup of patients who entered into the maintenance study and who were taking sertraline during the acute phase. In addition, means and standard deviations for these measures were obtained for the acute and continuation phase for patients taking sertraline who entered the continuation phase.

Multiple regression analysis was performed to explore the effect of baseline and clinical demographics on baseline Q-LES-Q total and CAPS-2 social/occupational impairment composite score. Table 1 shows the independent variables entered into the model: baseline CAPS-2 severity, presence of comorbid depression, gender, age, history of childhood trauma, type of trauma, duration of illness, and presence of comorbid major depression.

Logistic regression was performed to examine the effect of baseline Q-LES-Q at the maintenance phase in predicting relapse, and the effect of Q-LES-Q in the acute phase in predicting response (CGI-I = 1 or 2), improved or very much improved, for each treatment group.

RESULTS

For the 2 pooled acute-treatment studies, 359 patients formed the intent-to-treat sample. The typical patient (see Table 1) was a white woman in her late 30s presenting with a chronic form of moderate-to-severe PTSD complicated, in 43% of cases, by concurrent major depression. Consistent with previous treatment research in civilian settings, the most common trauma category was physical or sexual assault.

QOL Improvement: Acute Phase

Acute sertraline treatment led to significant improvement in Q-LES-Q scores when compared to placebo (Table 2). Sertraline resulted in rapid normalization of Q-LES-Q scores: 58% of sertraline-treated patients who met responder criteria achieved a Q-LES-Q score within 10% of the mean of the community norm data. It is interesting that the presence of comorbid depression was associated with a modest but nonsignificant reduction in acute improvement in the Q-LES-Q during sertraline treatment (improvement score with comorbid depression, 9.7 ± 3.9 vs. 13.2 ± 2.7 without comorbid depression; p = .48).

Functional Improvement: Acute Phase

Acute sertraline treatment led to significant improvement compared to placebo in the emotional role function-

Table 2. Effect of 12 Weeks of Acute Sertraline Treatment on Quality of Life and Functional Measures (LOCF endpoint) of 352 Patients[a]

	Sertraline		Placebo		
Scales	N	Mean Score	N	Mean Score	p Value
Q-LES-Q total score[b]	140		145		
Baseline		54.1		56.2	
Endpoint		66.1		61.4	.010
SF-36 emotional role functioning subscale score[b]					
With comorbid depression	35		38		
Baseline		25.7		27.2	
Endpoint		62.4		52.3	.265
No comorbid depression	64		67		
Baseline		35.9		36.8	
Endpoint		61.8		40.5	.002
SF-36 mental health subscale score[b]					
With comorbid depression	35		39		
Baseline		36.2		38.9	
Endpoint		62.4		58.6	.473
No comorbid depression	64		67		
Baseline		45.4		48.1	
Endpoint		59.9		51.5	.032
CAPS-2 social/occupational impairment composite score[c]	178		174		
Baseline		4.4		4.5	
Endpoint		2.8		3.1	.038

[a]Abbreviations: CAPS-2 = Clinician-Administered Posttraumatic Stress Disorder Scale, Part 2; LOCF = last observation carried forward; Q-LES-Q = Quality of Life Enjoyment and Satisfaction Questionnaire; SF-36 = Medical Outcome Study 36-Item Short Form. Ns vary due to missing data.
[b]Higher score is more improved.
[c]Higher score is more impaired.

ing and mental health SF-36 subscales (see Table 2). As with the Q-LES-Q data, the presence of comorbid depression did not have a significant effect on SF-36 factor improvement. Acute sertraline treatment was also associated with significantly greater improvement in CAPS-2 social/occupational impairment composite scores than placebo treatment (see Table 2).

QOL/Functional Improvement

Continuation phase. There was modest but progressive QOL and functioning improvement during the open-label continuation phase that was coincident with improvement in PTSD symptom severity. When the subgroup of patients treated with sertraline during both acute and continuation phases was analyzed (Table 3), approximately 20% of the overall QOL/functional improvement was found to occur during the continuation phase.

Double-blind relapse prevention phase. Double-blind substitution of placebo in this chronically ill group of PTSD patients resulted in significant clinical deterioration or relapse; almost 50% of patients experienced significant increase in the CAPS-2 severity score.[31] In contrast, efficacy was largely sustained among patients who continued on treatment with sertraline across 28 additional weeks of the relapse prevention phase of the study. Parallel with deterioration in PTSD symptoms, patients switched to placebo lost some (but not all) of the gains they had made both in QOL (Figure 2) and functional measures (Figure 3).

Exploratory Analyses

Correlates of QOL/functional impairment at baseline. Patients were significantly impaired in both QOL and functioning as indicated by their baseline scores on the Q-LES-Q and the CAPS-2 social/occupational composite score (see Table 1). A multiple regression analysis was performed (Table 4), using the baseline scores on each scale as the dependent variable, in an attempt to identify demographic and clinical variables that were contributing to impairment. The results, which were consistent for both QOL and functional impairment, found PTSD severity as measured by the CAPS-2 total severity score to be the largest single determinant of impairment. The presence of comorbid depressive disorder (primarily major depression) contributed significantly ($p = .0001$), though only modestly, to the model. Gender, current age, history of childhood trauma, type of trauma, duration of illness, and high levels of Axis I comorbidity (2 or more diagnoses) did not explain statistically significant amounts of the variance.

Consistent with the modest role that comorbid depression appears to play in contributing to QOL impairment, the mean Q-LES-Q score at baseline in patients with comorbid depression was slightly lower than in patients without comorbid depression (51.9 vs. 58.7).

QOL status as a predictor of treatment response. An exploratory logistic regression analysis was performed to examine whether severity of impairment in QOL at baseline was a predictor of acute phase treatment response, defined as a week-12 CGI-I score ≤ 2 (much or very much improved). The odds ratio (1.003) for achieving responder status for patients with lower baseline Q-LES-Q scores was virtually identical for patients with only mild QOL impairment ($p = .81$).

We also examined whether the degree of impairment in QOL at maintenance phase baseline increased the risk of relapse in patients who continued on either sertraline treatment or placebo. A logistic regression analysis found that maintenance phase baseline Q-LES-Q scores had no predictive value (sertraline odds ratio, 0.964, $p = .39$; placebo odds ratio, 0.962, $p = .26$).

DISCUSSION

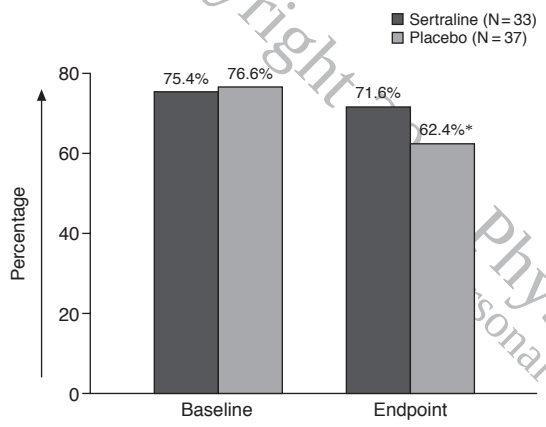
In the current treatment sample, PTSD was found to be associated with a level of QOL impairment, as measured by the Q-LES-Q and the SF-36 emotional role functioning and mental health subscales, that was greater than has been reported for panic disorder and approached that of patients with severe, chronic forms of depression.[1,4] Psychosocial functioning, as measured by the illness-specific scale, the CAPS-2 social/occupational impairment composite, was similarly impaired.

Table 3. Effect of Continuation Treatment on Quality of Life/Functional Measures: Results for a Subgroup of 47 Patients Who Received Sertraline Throughout Both the Acute and Continuation Phases of Treatment[a]

Scales	Acute Baseline	Week 12	Week 36	Percent of Week 36 Improvement That Had Occurred by Week 12
Q-LES-Q, percent of total score	55.5 ± 10.3	71.4 ± 16.2	75.8 ± 12.8	78.3
CAPS-2 social/occupational impairment composite subscale	4.2 ± 1.3	1.8 ± 1.7	1.1 ± 1.3	77.4
SF-36, emotional role functioning subscale	34.0 ± 36.4	64.5 ± 38.2	67.4 ± 35.1	91.3
SF-36, mental health subscale	40.2 ± 15.9	64.6 ± 24.1	73.2 ± 16.6	73.9

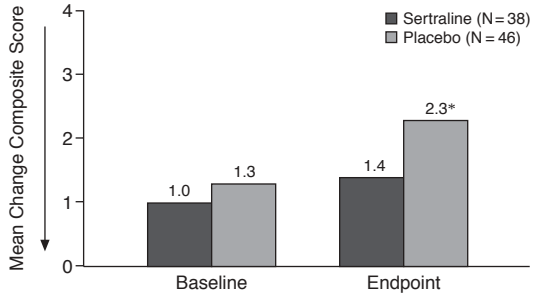
[a]Abbreviations: CAPS-2 = Clinician-Administered Posttraumatic Stress Disorder Scale, Part 2; Q-LES-Q = Quality of Life Enjoyment and Satisfaction Questionnaire; SF-36 = Medical Outcome Study 36-Item Short Form.

Figure 2. Adjusted Quality of Life Enjoyment and Satisfaction Scale (Q-LES-Q) Total Scores After 28 Weeks of Double-Blind Relapse Prevention Phase



*p < .02.

Figure 3. Adjusted Mean Change in Clinician-Administered Posttraumatic Stress Disorder Scale, Part 2 (CAPS-2), Social/Occupational Impairment Composite Score During 28 Weeks of Double-Blind Relapse Prevention Phase



*p < .02.

Despite the severity of QOL impairment and the chronicity of PTSD illness (mean duration > 10 years), patients treated with sertraline showed significant improvement during acute treatment in all QOL and functional measures assessed in this study (Table 2). Approximately 3 of 5 patients who responded acutely to sertraline had Q-LES-Q scores equivalent to the community norm by week 12. These results are consistent with previous findings in depression and anxiety disorders, for which the largest proportion of QOL/functional improvement has been noted during acute treatment.[4,41] The presence of a comorbid depression was associated with a modest, but not statistically significant, reduction in the degree of improvement in QOL and psychosocial functioning during the first 12 weeks of treatment.

Table 4. Determinants of Baseline Impairment in Quality of Life and Functioning: Results of Hierarchical Multiple Regression Analysis[a]

Step and Variable	Partial R^2	Model R^2	Variance Ratio Test (F)	p Value
Baseline Q-LES-Q score				
Step 1: Baseline Q-LES-Q total score	0.248	0.248	114.802	.0001
Step 2: Comorbid depression diagnosis	0.037	0.285	18.012	.0001
Step 3: Type of trauma (sexual assault vs all other)	0.006	0.292	3.115	.078
Step 4: Time from traumatic event	0.005	0.296	2.333	.128
Step 5: Duration of illness	0.005	0.301	2.355	.126
Baseline CAPS-2 occupational/ social impairment composite score				
Step 1: Baseline CAPS-2 total score	0.250	0.2497	116.485	.0001
Step 2: Comorbid Axis I depression	0.019	0.2683	8.888	.003
Step 3: Gender	0.002	0.270	–1.354	.390

[a]Abbreviations: CAPS-2 = Clinician-Administered Posttraumatic Stress Disorder Scale, Part 2; Q-LES-Q = Quality of Life Enjoyment and Satisfaction Questionnaire.

Continuation treatment with sertraline yielded 20% further improvement in QOL and psychosocial measures. The rapidity of QOL improvement during acute treatment suggests that there may be a nonlinear relationship between improvement in symptom severity and improvement in QOL. Although speculative, we postulate that initial reduction from relatively severe levels of symptom severity may yield disproportionately larger QOL improvement than the same degree of improvement at the milder end of the symptom severity spectrum. There may be a symptom severity threshold below which other factors in an individual's life take over and become primary determi-

nants of QOL. The relationship between QOL measures and illness-specific symptom measures is an area that deserves further research.

In patients who were discontinued from sertraline, recurrence of PTSD symptomatology was associated with a rapid worsening in QOL and functional measures. It should be noted, though, that among patients treated with placebo who suffered recurrence of PTSD symptoms, the severity of symptoms, and the degree of QOL and psychosocial impairment, were still notably less than at entry into the acute phase of the study. All patients had been treated with open-label sertraline for a minimum of 24 weeks prior to entering the double-blind discontinuation study, which may have had some protective effect, thus preventing a full relapse during the double-blind discontinuation phase. This would be consistent with a similar finding by our group[41] of low relapse after discontinuation of long-term sertraline treatment of panic disorder.

The results of an exploratory regression analysis found that the severity of PTSD symptomatology, as measured by the CAPS-2, was the most significant determinant of QOL and functional impairment, contributing approximately 25% of the variance in both instances, while chronicity and comorbidity accounted for relatively little of the variance. These intriguing exploratory observations require replication and more extensive investigation.

Additional exploratory analyses examined the predictive value of baseline QOL impairment. The results suggested that the severity of QOL impairment at baseline did not predict reduced response to 12 weeks of acute treatment. Furthermore, residual QOL impairment at the baseline of the maintenance phase of treatment did not predict an increased risk of relapse upon sertraline discontinuation.

The limitations of the current study include the restrictiveness of the entry criteria into the acute study, especially limitations on Axis I comorbidity, most notably alcohol and substance abuse. Though such exclusion criteria are typically in clinical trials, they limit the generalizability of the study results to "real life" clinical situations in which PTSD comorbidity is the rule rather than the exception.[7] A second limitation of the current study is the attrition observed over the long-term course of the study. Though this is to be expected, it is uncertain what bias has been introduced. For example, more than one third of the patients who discontinued during the continuation phase met responder criteria at the time of electing to discontinue the study. A third possible concern might be the small amount of the total variance accounted for by the demographic and clinical variables employed in the regression models. There are at least 2 nonexclusive explanations for this finding. First, QOL and functional impairment might well be outcome factors that are relatively orthogonal to traditional symptom-based rating measures. Therefore, one would expect limited overlap between these factors. Second, it should be remembered that the Q-LES-Q and the CAPS-2 social/occupational impairment composites are imperfect proxy measures for the domains that they are intended to measure. Though they have been shown to be valid and reliable measures, they still lack precision, and this lack of precision constitutes a "ceiling" on the ability to identify correlates and determinants of QOL/functional impairment. In light of this statistical restriction, a 25% contribution may be viewed as a substantial degree of predictive value.

CONCLUSION

The results of this study suggest that PTSD is associated with a substantial degree of QOL and functional impairment that derives, at least partially, from the severity of specific PTSD symptomatology, and minimally from the chronicity of the illness or from the presence of a concurrent major depression. More severe QOL and functional impairment at baseline did not predict a reduced treatment response to sertraline in PTSD. In fact, acute treatment led to rapid and significant improvement in QOL and psychosocial functioning, which was only minimally reduced by the presence of comorbidity. Continued treatment led to progressive and sustained improvement in QOL and functioning, which was partially lost upon double-blind discontinuation of sertraline.

Further research will be needed to determine how to effectively manage the subset of patients who do not achieve a symptomatic and QOL response to pharmacotherapy of their PTSD. The current data, though requiring replication with other SSRIs, suggest that sertraline monotherapy for PTSD rapidly improves patients' QOL and psychosocial functioning.

Drug name: sertraline (Zoloft).

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