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The Functional Impact of Subsyndromal Depressive Symptoms in Bipolar Disorder: Data from STEP-BD

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Abstract

Background—This report describes baseline characteristics and functional outcomes of subjects who have prospectively observed subsyndromal symptoms after a major depressive episode (MDE).

Methods—All subjects were participants in the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). We identified subjects with at least 2 years of observation whose prior or current episode was a MDE, and who were in a stable clinical state of either recovered (no more than 2 moderate symptoms for at least 8 weeks), a MDE by DSM IV criteria, or with continued subsyndromal symptoms. The subsyndromal group was defined *a priori* as 3 or more moderate affective symptoms but without meeting diagnostic criteria for major depression.

Results—The final cohort included 1094 recovered, 112 subsyndromal, and 310 individuals in a MDE. The average time spent in each clinical status ranged from 120 to 132 days. The subsyndromal group was most similar to those in a MDE, differing only on the intensity of depressive symptoms and the number of work days missed due to ongoing symptoms. Reported sadness, inability to feel and lassitude were each associated with multiple measures of impairment.

Limitations—This study is limited by the cross sectional approach to defining outcomes.

Conclusions—These findings are consistent with studies in unipolar major depression that indicate that functional impairment observed in the context of subsyndromal depressive symptoms is

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comparable to that of a full episode. This work underscores the need to include subsyndromal symptoms in study outcomes and to target full remission in clinical practice.

Keywords

bipolar disorder; subsyndromal depressive symptoms; depression; function

Introduction

People with bipolar disorder have episodically impaired psychosocial functioning (Coryell et al 1993; Bauwens et al 1991; Gitlin et al 1995; Bauer et al., 2001; Altshuler et al 2002; Calabrese et al 2003), and some degree of functional impairment is evident even during remissions (Cooke et al. 1996; Shapira et al 1999; MacQueen et al. 2000). MacQueen and colleagues (2001) reported that up to 60% of individuals with bipolar disorder do not regain full functioning in occupational and social domains (MacQueen et al. 2001). Ongoing depressive symptoms are the strongest predictor of functional deficits in persons with bipolar disorder (Bauer et al., 2001; Judd et al., 2005). While recurring episodes of depression are clearly associated with poor outcomes, relatively less is known about the impact of subsyndromal depressive symptoms, or depressive symptoms of insufficient number, duration, and/or intensity to meet criteria for a full depressive mood episode. The presence of subsyndromal symptoms after resolution of a major affective episode is associated with increased risk for relapse (Perlis et al., 2006; Judd et al., 2008). The current investigation is concerned with the relationship of persistent subsyndromal symptoms to functional outcomesGiven that people with bipolar disorder spend approximately one third of their adult lives with depressive symptoms (Judd et al., 2002; 2003), the impact of depressive symptoms on functional outcomes is particularly relevant. In a study following patients for 2–4 years, almost half of those who did not experience full episodic relapse experienced significant affective symptoms. In contrast to relapse rates, a measure of cumulative affective morbidity was the strongest predictor of functional outcome in this study (Gitlin et al 1995). Similarly, Bauer et al (2001) reported that both number of weeks in a full depressive episode and average depression symptom score (including subsyndromal symptoms) were significantly related to functional outcomes. Two studies of euthymic patients in ongoing care demonstrated relationships between subsyndromal HAM-D scores and social adjustment (Shapira et al., 1999) and function (Cooke et al., 1996). A small study of 25 men with bipolar disorder indicated a relationship between subsyndromal depressive symptoms and function as measured by the GAF (Altshuler et al., 2002). In order to further elucidate the relationship between subsyndromal depressive symptoms, social and vocational function, and quality of life in bipolar disorder, we examined these variables in participants in the Systematic Treatment Enhancement Program for Bipolar Disorder (“STEP-BD”; Sachs et al., 2003).

Methods

STEP-BD is a large, NIMH-funded longitudinal study that encompassed standardized assessments and treatments of adult outpatients with bipolar affective disorder. The methods of STEP-BD are described in detail elsewhere (Sachs et al, 2003); what follows is a summary of procedures relevant to the current report.

STEP-BD Inclusion and Exclusion Criteria

Eligibility criteria were broadly inclusive in order to maximize the generalizability of study results. Patients were at least 15 years of age, met DSM-IV criteria for bipolar I, bipolar II, bipolar NOS, or schizoaffective disorder with manic or bipolar subtypes. Patients entered the study in any mood state. Exclusion criteria were limited to the unwillingness or inability to

comply with study assessments, or inability to give informed consent. The study was approved by the institutional Human Subject Review Board of each site and all patients gave written informed consent before enrollment in the study.

STEP-BD Measures and Procedures

Investigators and clinicians at all study sites received standardized training and met certification requirements on the study measures and assessment tools. To prevent rater drift, every six months randomly selected clinical status ratings (see below) were reviewed, with remedial training administered as necessary. DSM-IV Axis I diagnoses were confirmed using the Mini International Neuropsychiatric Interview (MINI Version 5.0) (Sheehan et al, 1998). Demographic and clinical course variables were routinely and systematically assessed by the Affective Disorders Evaluation (ADE; Sachs 2003). The current clinical status of the patients was determined by a semi-structured diagnostic instrument, the "Clinical Monitoring Form" (CMF) (Sachs et al, 2003) based on DSM-IV criteria. The eight operationally defined clinical states were *depression*, *mania*, *hypomania*, *mixed episode*, *recovering* (≤2 affective symptoms with moderate or greater severity for less < 8 weeks), *recovered* (≤2 affective symptoms with moderate or greater severity for ≥ 8 weeks), *continued symptomatic*, and *roughening* (worsening observed after achievement of a recovered state). The categories of continued symptomatic and roughening are viewed as subsyndromal states in which patients have at least 3 moderate affective symptoms, but do not meet criteria for a full affective episode. Continued symptomatic is coded if the patient had not reached recovered status following a full mood episode, whereas roughening is coded if the patient had previously recovered from the most recent syndromal episode and developed new symptoms but not to the level of a new syndromal episode. In the current investigation, we were most interested in assessing the differences between patients who were recovered, depressed, or continued symptomatic following a major depressive episode (indicating partial recovery from that episode). The clinical monitoring form is used at each psychiatric follow-up visit; the frequency of visits is clinically determined.

Participants also complete more extensive independent ratings quarterly over the first year, and every six months after for the duration of their participation in STEP-BD. The intensity of manic and depressive symptoms was assessed using the Young Mania Rating Scale (YMRS, range 0–60) (Young *et al*, 1978) and Montgomery-Asberg Depression Rating Scale (MADRS, range 0–60) (Montgomery and Asberg, 1979). Functional impairment over the last 7 days prior to evaluation was assessed with the Range of Impaired Function Tool (LIFE-RIFT) (Leon *et al*, 1999 and 2000). The LIFE-RIFT is a brief, semi-structured, clinician administered scale that assigns scores from 1-no impairment, 3-moderate/fair to 5-severe impairment to four areas of function (work/role performance, interpersonal relationships, recreation and satisfaction with activities). Overall function score ranges from 4 to 20. The reliability and validity of LIFE-RIFT has been established in BD with high interrater reliability (intraclass correlation coefficient, ICC: 0.99) and concurrent validity (correlation between LIFE-RIFT total score and GAS (b = −0.03; 95% CI: −0.04 to −0.02; $z = 4.88$, $p < 0.001$; $R^2 = 0.39$; $N = 153$ subjects; observations = 538) (Leon *et al*, 2000). Work disability was assessed by determining (1) how many of the last 30 days the patients were unable to work (job or other role functions) at all ("Work Days Missed") due to their mental health status including drug and alcohol use; (2) how many days over the last 30 days patients had to cut down or did not get done as much work as expected when they are fully functional ("Work Days Impaired"). The short form of the Quality of Life and Enjoyment Scale (Q-LES-Q) is a 16-item self-report questionnaire assessing the degree of enjoyment and satisfaction in a variety of areas of daily functioning (Endicott et al., 1993). Higher scores indicate greater life satisfaction. Personality was assessed using the NEO-Five Factor Inventory (NEO-FFI) (Costa and McCrae, 1988 and 1992) and the Personality Disorder Questionnaire (PDQ-4) (Hyler et al, 1988).

Identification of Cohort for the Current Study

Beginning with the 4360 individuals enrolled in STEP-BD through 5/31/05, those with less than 2 years of longitudinal follow-up were excluded. Remaining participants were grouped by those with stable clinical status assessments of either depressed, recovered, or continued symptomatic (i.e., subsyndromal) at some point over their first two years of participation in STEP-BD. Stability was defined as two consecutive CMFs with the same clinical status; average time in stable clinical status ranged from 120–132 days). Given the fact that residual hypomanic or manic symptoms do not appear to have the same strong association with functional deficits as depressive symptoms (Judd et al., 2005), those patients in the "continued symptomatic" group whose most recent episode was hypomanic, manic, or mixed were excluded from the analysis. Additionally, because "roughening" represents increase in symptoms after a period of recovery, and those with this clinical picture may be different from those who never fully recover from depressive episodes, these subjects were also excluded. After defining the cohort of subjects in the recovered, depressed and subsyndromal groups, we looked at measures of functional outcomes at the first follow-up visit after the second of the two visits required for stable clinical status. The functional assessment was required to be within 90 days of the first visit in a stable clinical state, with the time between the last clinical visit (CMF) and the functional outcome measures less than or equal to 7 days. This resulted in three groups: recovered (n=1094), depression (n=310), and subsyndromal symptoms following MDE (n=112).

Means and standard deviations were reported for continuous variables and percentages for discrete variables. Analysis of variance and chi-square methods were used to compare demographic and clinical characteristics, and analysis of variance and analysis of covariance methods were used to compare symptom severity, function and quality of life measures across the three disease states. If significant differences ($p<.05$) were identified, post-hoc comparisons with Bonferroni corrections were conducted. Spearman's rank correlation coefficients were estimated to assess the relationship between individual depressive symptoms on the MADRS and the measures of function and quality of life.

RESULTS

Sample Characteristics at Study Entry

The patient population was predominantly Caucasian (90.6%). Fifty-seven percent were female, and 66% had bipolar I disorder. There was no difference in group membership related to diagnosis of bipolar I, bipolar II, or other diagnoses of bipolar disorder. There were some observed differences between groups on baseline characteristics, including mean duration of illness, relationship status, and education and income. Additionally, those in the recovered, subsyndromal, and depressed groups differed significantly on all clinical measures, including number of previous episodes, presence of comorbid conditions, rapid cycling, and/or psychosis, and personality as measured by the NEO-PI and PDQ.

Table 2 presents unadjusted group differences on measures of clinical symptoms (MADRS and YMRS) and functional status (LIFE-RIFT total and subscales, work days missed, work days impaired, and Q-LES-Q scores). In table 3, we present group differences for the same set of variables, but adjust for all significant group differences in baseline demographic and clinical characteristics (duration of illness, lifetime number of episodes total, manic, and depressive, years of educational, income, relationship status, presence of comorbid alcohol and substance abuse, anxiety disorders, ADHD, rapid cycling, and psychosis, NEO-PI scale scores, and PDQ total score). Therefore, Table 3 includes adjusted means, and the independent impact of clinical status on each variable after adjusting for significant group differences. In each case, clinical

status is independently associated with scores on each of these clinical and functional variables, after controlling for all other group differences.

Clinical and Functional Characteristics by Group

Pairwise group comparisons of the adjusted means are noted in Table 3. As expected, the recovered and depressed groups differed on total MADRS scores, measuring severity of depression. They did not differ on hypomanic or manic symptoms, as measured by the YMRS. The recovered and depressed groups differed significantly from each other on all other functional outcome measures.

Those with subsyndromal symptoms also differed substantially from those in the recovered group, with higher symptom scores for measures of depression and mania. They reported greater functional impairment on the total LIFE-RIFT and within each individual domain of Satisfaction, Recreation, Work, and Relationships. Those with subsyndromal symptoms experienced more impaired work days than those in the recovered group, but did not report more missed days of work. They also reported less overall satisfaction with the quality of their daily life (Q-LES-Q) than those in the recovered group.

The subsyndromal group differed from those in the depressed group only on intensity of depressive and hypomanic/manic symptoms and in work days missed. While those in full depressive episodes reported more severe depressive symptoms, those in the subsyndromal group reported more hypomanic and manic symptoms. Those experiencing a full depressive episode missed more work days due to their illness.

Individual Symptoms and Function

In order to assess the relationship between individual clinical symptoms and functional outcomes, we assessed the relationship between individual MADRS items and functional outcomes (LIFE-RIFT total, Q-LES-Q, work days missed, work days impaired) for those patients in the subsyndromal group only (see Table 4). The MADRS item of reported sadness was the only individual item to be significantly associated with scores on all functional outcome measures (r^2 range from .17–.43). Lassitude and inability to feel were associated with LIFE-RIFT total score (r^2=.25 and .36, respectively). Inability to feel was associated with the number of work days impaired (r^2=.27). Pessimistic thoughts, suicidal thoughts, inability to feel, lassitude, concentration difficulties, inner tension, and apparent sadness were also associated with Q-LES-Q scores (r^2 range from .25–.43). Thus, reported sadness was associated with four adverse outcomes, inability to feel with three and lassitude with two.

Individual YMRS scores were low, with the highest scores for ‘irritability’ (mean = 2.13; SD=1.75) and ‘speech (rate and amount)’ (mean=1.24; SD=1.69). All other YMRS items had an average score less than one.

DISCUSSION

To our knowledge, this is the first investigation to examine baseline characteristics and prospective functional outcome across a large group of well-characterized patients with bipolar disorder experiencing sustained recovery, depressive episodes, and chronic subsyndromal symptoms.

Our findings are consistent with previous work that suggests that continued subsyndromal symptoms after a major depressive episode adversely affect functional recovery in patients with bipolar disorder (Gitlin et al., 1995; Bauer et al., 2001; Shapira et al., 1991; Cooke et al., 1996; Altshuler et al., 2002) and unipolar major depression (Rapaport et al., 2002, Howland et al., in press, Judd et al., 1998). More specifically, patients with sustained continued

symptoms experience essentially the same functional burden as those experiencing a full episode of depression. Particularly salient symptoms that appear to correlate with impairment in individuals with persistent subsyndromal symptoms are reported sadness, anhedonia and lassitude. This suggests that clinicians should be particularly mindful of the persistence of these symptoms and any associated impairment should be the focus of continued aggressive treatment.

While group status (recovered, depressed, subsyndromal) was defined by prospective observation of a sustained clinical status rating over at least 2 years of observation in STEP-BD, the groups did differ on multiple baseline characteristics. Generally, the subsyndromal and depressed groups were more similar, and differed from those in the recovered group. Those who ultimately achieved recovered status had a shorter duration of bipolar disorder, fewer total episodes, less evidence of personality disorder, and were less likely to have comorbidity and rapid cycling than those who were in the depressed and continued symptomatic groups. Similar to rates observed in other studies, 54% of those in the subsyndromal group met criteria for a comorbid anxiety disorder (MacQueen et al., 2003). Compared to the recovered and depressed groups, the subsyndromal group had the highest levels of comorbidity overall, and the greatest number of comorbid diagnoses of ADHD, anxiety, and substance use disorders.

Across bipolar subtypes, patients diagnosed with bipolar I, II, or other bipolar diagnoses were similarly likely to experience sustained periods of recovery, subsyndromal symptoms, or depression. This is consistent with recent work from the Collaborative Depression study (Judd et al., 2008), and highlights the chronicity, severity and functional burden associated with all bipolar spectrum diagnoses. Interestingly, more individuals in the recovered group reported a previous diagnosis of a psychotic disorder. This history may have resulted in more aggressive treatment for these individuals, or may be a marker for a more treatment responsive phenotype.

However, functional outcomes remained significantly different across the three groups after accounting for these baseline differences. As expected, the recovered and depressed groups differed on almost all measures, with the exception of mean YMRS score. Interestingly, those in the subsyndromal group presented with the highest adjusted YMRS score. It is possible that patients who are likely to experience sustained periods of subsyndromal symptoms are prone to mixed episodes, or to a mixed symptom presentation, complicating treatment course and decisions (Goodwin et al., 2004; Keller et al., 1986; Strakowski et al., 1996). In a recent analysis, 26.7% of those experiencing subsyndromal symptoms after recovery from a major affective disorder had symptoms of mixed polarity (Judd et al., 2008), a pattern that has been observed elsewhere (Bauer et al., 2005; Suppes et al., 2005). It is possible that antidepressant exposure contributes to the experience of mixity in these patients (Goldberg et al., 2007). Further work may help establish the frequency and characteristics of those likely to experience of subsyndromal mixed depressive and hypomanic/manic symptoms, and the relationship of these symptoms to clinical and functional outcomes.

Similar to patients in sustained depressive episodes, those patients with prolonged periods of subsyndromal symptoms separated from those in the recovered group on almost all of the functional outcome measures. They reported greater functional impairment on the total LIFE-RIFT and within each individual domain of Satisfaction, Recreation, Work, and Relationships, more impaired work days than those in the recovered group, and less overall satisfaction with the quality of their daily life.

The only exception was the measure of the number of work days missed. Those in a depressive episode were most likely to miss work due to symptoms, compared to those with continued symptoms or those who were recovered. However, though improvement may allow patients

with continued symptoms to work, they perform consistently at lower levels, a problem described as “presenteeism” (Adler et al, 2006).

The strengths of this analysis include the large, “real world” nature of the sample. One of the weaknesses is the cross-sectional nature of this initial work. Longitudinal outcome data would be beneficial in the future. Rapaport has reported that symptom severity, comorbid diagnoses, and other relevant clinical factors account for no more than a quarter of the variance in quality of life in any DSM IV mood and anxiety disorders previously evaluated (Rapaport et al., 2005). Since the major focus of this paper is the relationship of subsyndromal symptoms to functioning rather than quality of life in bipolar disorder, we did not focus our analyses on the relationships between quality of life and symptom status across the range of mood states.

In conclusion, patients with sustained subsyndromal symptoms were indistinguishable from those in a full depressive episode on all measures of functional outcomes. The current work reinforces the need to attempt multiple trials of medication and medication combinations to strive toward full recovery in all patients and to include subsyndromal symptoms and/or functional outcomes in clinical trials.

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Table 1

Baseline Demographic and Clinical Characteristics, by Group*

	Recovered (n=1094)	Subsyndromal Depression c (n=112)	Syndromal Major Depressive Episode (n=310)	
Demographic Variables				
				Kruskal Wallis Chi-Square
Mean Age, years (SD)	41.06 (12.91) N=1094	40.29 (12.20) N=112	41.76 (11.27) n=310	χ^2=2.36 p=0.3076
Mean duration of illness, years (SD)	22.68 (13.06)	24.15 (12.14)	25.4 (12.14)	χ^2=12.28 **p=0.0022**
Mean Days Between CMFs (SD)	123.52 (44.37)	120.31 (33.09)	125.16 (64.37)	χ^2=2.24 p=0.33
				Chi-Square
Female (n, %)	607 55.54%	67 59.82%	185 59.68%	χ^2=2.17 p=0.34
Relationship status (n,%)				
Single	379 (36.13%)	36 (33.96%)	86 (30.07%)	χ^2=10.83
Separated, Div., Wid	432 (41.18%)	41 (38.68%)	109 (38.11%)	df=4
Married/Comtd Reltshp	238 (22.69%)	29 (27.36%)	91 (31.82%)	**p=0.03**
Diagnosis (n, %)				
BDI	733 (67.06%)	70 (62.50%)	198 (63.87%)	χ^2=2.33
BDII	273 (24.98%)	31 (27.68%)	88 (28.39%)	df=4
Other	87 (7.96%)	11 (9.82%)	24 (7.74%)	p=0.68
Race/Ethnicity (n,%)				
Caucasian	995 (91.03%)	97 (86.61%)	279 (90.00%)	χ^2=2.43
Other	98 (8.97%)	15 (11.81%)	31 (10.00%)	df=2
				p=0.30
Education (n,%)				
7th-high school	137 (13.09%)	22 (20.75%)	52 (18.31%)	χ^2=28.89
some college	351 (33.52%)	45 (42.45%)	124 (43.66%)	df=4
college/graduate	559 (53.39%)	39 (36.79%)	108 (38.03%)	**p<0.0001**
Income (n,%)				
<$10,000	134 (14.61%)	14 (14.43%)	50 (19.92%)	χ^2=18.5
$10,000–$29,999	221 (24.10%)	36 (37.11%)	78 (31.08%)	df=4
>=$30,000	562 (61.29%)	47 (48.45%)	123 (49.0%)	**p=0.001**
Clinical Variables				
Number of previous episodes - Total (n,%)				
<3	90 (12.26%)	5 (6.76%)	7 (3.85%)	χ^2=28.77
3–9	273 (37.19%)	18 (24.32%)	50 (27.47%)	df=4
≥10	371 (50.54%)	51 (68.92%)	125 (68.68%)	**p<0.0001**
Depressive (n, %)				
<3	185 (16.91)	11 (9.82)	25 (8.06)	χ^2=56.14
3–9	322 (29.43)	25 (22.32)	48 (15.48)	df=4

	Recovered (n=1094)	Subsyndromal Depression c (n=112)	Syndromal Major Depressive Episode (n=310)	
Demographic Variables				
				Kruskal Wallis Chi-Square
≥10	587 (53.66)	76 (67.86)	237 (76.45)	**p<0.0001**
(Hypo)manic (n, %)				
<3	206 (18.83)	15 (13.39)	39 (12.58)	χ^2=29.18
3–9	346 (31.63)	26 (23.21)	68 (21.94)	df=4
≥10	542 (49.54)	71 (63.39)	203 (65.48)	**p<0.0001**
Alcohol abuse/ dependence (n, %)	379 37.6%	44 43.56%	129 45.91%	χ^2=7.01 **p=0.03**
Substance abuse/ dependence (n, %)	103 10.21%	17 16.83%	37 13.17%	χ^2=5.27 **p=0.07**
Any Anxiety disorder (n, %)	274 (27.13%)	55 (54.46%)	151 (53.36%)	χ^2=86.69 **p<0.0001**
ADHD (n, %)	54 (5.36%)	18 (17.82%)	25 (8.87%)	χ^2=23.94 **p<0.0001**
Rapid cycling past year (n, %)	165 (15.85%)	30 (27.78%)	85 (30.04%)	χ^2=33.49 **p<0.0001**
History of Psychosis (n,%)	460 (43.11%)	35 (31.53%)	88 (29.73%)	χ^2=20.59 **p<0.0001**
NEO-PI (mean, SD)				
Agreeableness	46.56 (12.15)	38.62 (11.45)	44.13 (12.34)	**χ2=31.08, p<0.0001**
Conscientiousness	40.24 (10.91)	37.10 (11.16)	36.23 (10.73)	**χ2=24.30, p<0.0001**
Extraversion	45.40 (11.22)	39.48 (11.43)	38.71 (10.96)	**χ2=57.70, p<0.0001**
Neuroticism	60.77 (10.58)	67.75 (8.0)	67.48 (8.18)	**χ2=91.01, p<0.0001**
Openness	55.77 (10.76)	53.10 (12.70)	52.61 (10.97)	**χ2=6.32, p=0.04**
PDQ (mean, SD)	30.48 (16.49)	43.77 (14.30)	41.23 (13.83)	χ2=93.41 **p<0.0001**

* Percentages are based on the number of subjects with complete data for each variable.

Table 2

Unadjusted Mean and Standard Deviation of Functional Outcomes at Assessment Visit following period of stable clinical status, by Group

	Recovered	Subsyndromal Depression	Syndromal Major Depressive Episode	Kruskal Wallis Chi Square df=2
MADRS	6.72 (6.52)	19.83 (7.93)	26.66 (8.67)	**$\chi 2=679.15$ p<0.0001**
YMRS	3.66 (4.34)	8.69 (6.89)	6.55 (5.53)	**$\chi 2=135.07$ p<0.0001**
LIFE-RIFT				
Total Score	9.04 (3.04)	13.18 (2.92)	14.81 (3.06)	**$\chi 2=505.69$ p<0.0001**
Satisfaction	2.12 (0.85	3.19 (0.87)	3.77 (0.93)	**$\chi 2=506.81$ p<0.0001**
Recreation	2.08 (1.11)	3.23 (1.14)	3.67 (1.14)	**$\chi 2=359.88$ p<0.0001**
Work	2.34 (1.17)	3.47 (1.19)	3.90 (1.10)	**$\chi 2=331.79$ p<0.0001**
Relationship	2.50 (1.13)	3.30 (1.25)	3.42 (1.28)	**$\chi 2=137.64$ p<0.0001**
Work Days Missed	1.08 (3.76)	4.20 (6.68)	8.61 (10.39)	**$\chi 2=278.38$ p<0.0001**
Work Days Impaired	3.95 (7.04)	8.62 (9.29)	11.28 (10.43)	**$\chi 2=162.21$ p<0.0001**
Q-LES-Q	66.41 (17.41)	40.70 (16.19)	32.18 (14.78)	**$\chi 2=337.23$ p<0.0001**

Table 3

Functional Outcomes per group, adjusted for significant between-group differences on demographic and clinical baseline variables

	Recovered	Subsyndromal Depression	Syndromal Major Depressive Episode	
MADRS[1,2] n=351	6.79	18.61	23.12	**F=114.28 p<.0001**
YMRS[2,3] N=353	3.64	8.11	4.82	**F=10.28 P=.0001**
LIFE-RIFT				
Total Score[1,2] N=345	9.16	12.96	13.68	**F=54.68 p<.0001**
Satisfaction[1,2] N=352	2.15	2.98	3.41	**F=46.89 p<.0001**
Recreation[1,2] N=351	2.16	3.34	3.24	**F=29.87 p<.0001**
Work [1,2] N=347	2.32	3.32	3.60	**F=31.09 p<.0001**
Relationship[1,2] N=353	2.58	3.36	3.45	**F=13.29 p<.0001**
Work Days Missed[1] N=353	1.23	3.18	5.98	**F=20.24 p<.0001**
Work Days[1,2] Impaired N=354	3.54	10.32	11.72	**F=34.29 p<.0001**
Q-LES-Q[1,2] N=236	65.03	39.62	36.58	**F=49.21 p<.0001**

Significant pairwise comparisons adjusted for multiple comparisons (p<.0167)

[1]Recovered vs. Depressed

[2]Recovered vs. Continued Symptomatic

[3]Continued Symptomatic vs. Depressed

Table 4

Spearman Correlation Coefficients between individual MADRS items and Functional Outcomes for Subsyndromal Depression Group only

	LIFE-RIFT Total	Work Days Missed	Work Days Impaired	Q-LES-Q
Reported Sadness	**0.27 p=0.0001**	**0.23 p=0.03**	**0.17 p=0.11**	**−0.43 p=0.0005**
Pessimistic Thoughts	0.13 p=0.24	0.03 p=0.80	0.01 p=0.89	**−0.36 p=0.004**
Suicidal Thoughts	0.13 p=0.23	0.03 p=0.75	−0.02 p=0.84	**−0.34 p=0.006**
Reduced Sleep	0.04 p=0.71	0.17 p= 0.11	0.08 p=0.45	−0.15 p=0.24
Inability to Feel	**0.36 p=.0005**	0.09 p=0.37	**0.27 p=0.007**	**−0.35 p=0.005**
Lassitude	**0.25 p=0.02**	0.17 p=0.11	0.15 p=0.15	**−0.33 p=0.008**
Concentration Difficulties	0.18 p=0.10	0.11 p=0.31	0.19 p=0.07	**−0.41 p=0.0008**
Inner Tension	0.01 p=0.89	0.06 p=0.54	0.11 p=0.31	**−0.39 p=0.001**
Reduced Appetite	0.03 p=0.77	0.06 p=0.55	−0.05 p=0.64	−0.16 p=0.22
Apparent Sadness	0.14 p=0.19	0.11 p=0.27	0.08 p=0.42	**−0.25 p=0.05**