

A descriptive analysis of quality of life using patient-reported measures in major depressive disorder in a naturalistic outpatient setting

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Accepted: 7 April 2012 / Published online: 29 April 2012
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Abstract

Purpose Major depressive disorder (MDD) negatively impacts different aspects of an individual's life leading to grave impairments in quality of life (QOL). We performed a detailed analysis of the interaction between depressive symptom severity, functioning, and QOL in outpatients with MDD in order to better understand QOL impairments in MDD.

Methods This cross-sectional study was conducted with 319 consecutive outpatients seeking treatment for DSM-IV-diagnosed MDD at an urban hospital-based outpatient

clinic from 2005 to 2008 as part of the Cedars-Sinai Psychiatric Treatment Outcome Registry, a prospective cohort study of clinical, functioning, and patient-reported QOL outcomes in psychiatric disorders using a measurement-based care model. This model utilizes the following measures: (a) Depressive symptom severity: Quick Inventory of Depressive Symptomatology-Self Report (QIDS-SR); (b) Functioning measures: Global Assessment of Functioning (GAF), Sheehan Disability Scale (SDS), Work and Social Adjustment Scale, and the Endicott Work Productivity Scale; and (c) Quality of Life measure: Quality of Life, Enjoyment, and Satisfaction Questionnaire—Short Form (Q-LES-Q).

Results QOL is significantly impaired in MDD, with a mean Q-LES-Q score for this study population of 39.8 % (SD = 16.9), whereas the community norm average is 78.3 %. Regression modeling suggested that depressive symptom severity, functioning/disability, and age all significantly contributed to QOL. QIDS-SR (measuring depressive symptom severity), GAF, and SDS (measuring functioning/disability) scores accounted for 48.1, 17.4, and 13.3 % (semi-partial correlation values) of the variance in Q-LES-Q, respectively.

Conclusions Our results show that impairment of QOL increases in a monotonic fashion with depressive symptom severity; however, depression symptom severity only accounted for 48.1 % of the QOL variance in our patient population. Furthermore, QOL is uniquely associated with measures of Functioning. We believe these results demonstrate the need to utilize not only Symptom Severity scales, but also Functioning and Quality of Life measures in MDD assessment, treatment, and research.

Keywords Major depressive disorder · Quality of life · Major depression · Health-related quality of life

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Abbreviations

BAI	Beck Anxiety Inventory
CS-PTR	Cedars-Sinai Psychiatric Treatment Outcome Registry
EWPS	Endicott Work Productivity Scale
GAF	Global Assessment of Functioning
IRB	Institutional Review Board
QIDS-SR	Quick Inventory of Depressive Symptomatology-Self Report
Q-LES-Q	Quality of Life, Enjoyment, and Satisfaction Questionnaire—Short Form
QOL	Quality of life
MDD	Major Depressive Disorder
SDS	Sheehan Disability Scale
WHO	World Health Organization
WSAS	Work and Social Adjustment Scale

Introduction

The World Health Organization (WHO) defines health as “a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity” [1]. Unfortunately, the majority of clinical and research efforts in psychiatry have been more attentive to the impact of interventions on symptom reduction than on well-being or quality of life (QOL). Psychiatric illnesses are strongly associated with impairment in QOL, frequently at levels that are equal to or exceed those of medical illnesses [2]. The traditional focus on symptom improvement in psychiatric care and research may have resulted in more emphasis being placed on symptom severity rather than including improvement in functioning and QOL.

Major depressive disorder (MDD) negatively impacts a myriad of facets of an individual’s life including functioning, satisfaction with work, relationships, leisure, physical health, sexual functioning, sleep patterns, future outlook, and overall sense of fulfillment or contentment with one’s life [3]. Studies have demonstrated that patients with MDD have significant impairments in QOL [2–5]. An analysis from the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study revealed that severity of depressive symptoms was significantly associated with poor health-related quality of life [6]. Rapaport et al. [7] demonstrated significant impairments in quality of life in subjects with a broad array of different depressive and anxiety disorders entering clinical trials. This study reported that illness-specific symptom severity was significantly associated with baseline QOL impairment, but it explained only a modest proportion of the variance in QOL as measured by the Quality of Life, Enjoyment, and Satisfaction Questionnaire—Short Form (Q-LES-Q) [7]. There is a growing

consensus that successful treatment should not only target symptom severity, but also impairment in functioning and QOL in leading to restoration of health [8–10].

Despite the extensive literature investigating QOL in psychiatric disorders, a detailed examination is needed for the interaction between psychiatric symptom severity, clinical characteristics, functioning, and QOL in treatment-seeking outpatients with MDD. The purpose of this study is to perform an in-depth analysis of the critical factors thought to influence QOL for individuals with MDD in an outpatient clinical practice. The first goal of this study was to investigate the impact that a variety of factors (that have been implicated usually by exploratory and secondary analyses) truly had on QOL. Thus, we explicitly sought to investigate the role that age, sex, ethnicity, recurrence, psychiatric comorbidity, and severity of depressive and anxiety symptoms had on QOL. Based on previously published work, we postulated that QOL impairment would be adversely affected by psychiatric symptom severity and speculated that QOL would be adversely affected by functional impairment [7–11]. Hence, the second goal was to investigate the relationship between symptom severity, functioning, and QOL.

Method

Recruitment method

Patients presenting for psychiatric evaluation and treatment at the Cedars-Sinai Medical Center are enrolled in the Cedars-Sinai Psychiatric Treatment Outcome Registry (CS-PTR), an ongoing research study to track the outcome of psychiatric interventions in a naturalistic clinical setting using measurement-based care. The study was approved by the Cedars-Sinai Medical Center Institutional Review Board (IRB), Los Angeles, California. Patients are evaluated using the Mini International Neuropsychiatric Interview (MINI) [12]. The evaluations are performed by psychiatric residents, psychology interns, and social work interns who have undergone a course on the MINI and DSM-IV diagnoses. Each interview is monitored by a psychiatrist through a one-way mirror. Since the MINI does not have personality disorder modules (except for antisocial personality disorder), personality disorders are diagnosed clinically by employing DSM-IV criteria. Final diagnoses are confirmed using consensus techniques by a team led by a senior faculty member. Patient-reported outcomes consisting of self-report measures of depressive and anxiety symptom severity, functioning, and QOL (as detailed in the next section) are collected at baseline and then on a quarterly basis. All data are de-identified and entered into a secure database maintained by a data manager who monitors data completeness and integrity.

Table 1 Measures of symptom severity, functioning, and quality of life

Name	Rater	No. of items	Item scale	Score range	Higher score is	Score interpretation and calculation
Symptom severity measures						
<i>QIDS-SR</i> Quick Inventory of Depressive Symptomatology-Self Report [13]	Self	16	0–3	0–27	Worse	Severity of MDD depressive symptoms is categorized based on the QIDS-SR scores as detailed by Rush et al. [13]: remission (score 0–5), mild (score 6–10), moderate (score 11–15), severe (score 16–20), or very severe (score > 20) Scoring: Total score = the highest score on any 1 of the 4 sleep items (1–4) + item (5) + the highest score on any 1 appetite/weight item (6–9) + items (10–14) + the highest score on either of the 2 psychomotor items (15 and 16)
<i>BAI</i> Beck Anxiety Inventory [14]	Self	21	0–3	0–63	Worse	Severity of anxiety symptoms is categorized based on the BAI scores as detailed by Beck and Steer [20]: minimal (score 0–7), mild (score 8–15), moderate (score 16–25), or severe (score 26–63) Scoring: sum of all items
Functioning measures						
<i>GAF</i> Global Assessment of Functioning [15]	Clinician	N/A	N/A	1–99	Better	Functioning is categorized based on the GAF scores as detailed by the DSM-IV-TR [15]: superior functioning/no symptoms (score 91–100), good functioning/absent/minimal symptoms (score 81–90), slight impairment in functioning/transient symptoms (score 71–80), some difficulty functioning/mild symptoms (score 61–70), moderate difficulty functioning/moderate symptoms (score 51–60), serious difficulty functioning/serious symptoms (score 41–50), major impairment in functioning/some impairment in reality testing/communication/mood (score 31–40), inability to function/serious impairment in reality testing/communication/mood (score 21–30), some danger to self/others/occasional inability to care for self (score 11–20), or persistent danger to self/others/inability to care for self (score 1–10) Scoring: find the range that matches symptom severity or functioning level, then identify the number within the selected range
<i>SDS</i> Sheehan Disability Scale [16]	Self	3	0–10	0–30	Worse	There is no recommended cutoff score, range from unimpaired (score of 0) to highly impaired (score of 30) Scoring: sum of all items
<i>WSAS</i> Work and Social Adjustment Scale [17]	Self	5	0–8	0–40	Worse	Functioning, in areas such as work, home management, private leisure, social leisure, and relationships, is categorized based on WSAS scores as detailed by Mundt et al. [17]: major functioning impairment (score > 20), significant functioning impairment (score 10–20), or within normal range (score < 10) Scoring: sum of all items
<i>EWPS</i> Endicott Work Productivity Scale [18]	Self	25	0–4	0–100	Worse	Range from no impairment (score of 0) to major impairment in work productivity (score of 100) Scoring: sum of all items
Quality of Life measure						

Table 1 continued

Name	Rater	No. of items	Item scale	Score range	Higher score is	Score interpretation and calculation
<i>Q-LES-Q</i> Quality of Life, Enjoyment, and Satisfaction Questionnaire—Short Form [19]	Self	16 (first 14 items used for scoring)	1–5	0–100	Better	Quality of life is categorized based on the Q-LES-Q scores as detailed by Endicott et al. [18], Rapaport et al. and Schechter et al. [7, 19]: QOL is considered impaired (scores less than 10 % of the community norm; mean = 78.3 % (SD = 11.3), that is, scores less than 70.5 %), or severe QOL impairment (scores of 2 or more standard deviations below the community norm, that is, scores less than 55.7 %) Scoring: for Q-LES-Q, the total score is calculated as the sum of scores from items 1 through 14 and is converted to a percentage where 100 would be the best score and 0 is the worst. The percentage score is reached using the following calculation: (Raw Score–Minimum Possible Score)/(Maximum Possible Score–Minimum Possible Score). The possible raw score is 14, and the best is 70, that is, Q-LES-Q percentage score = (Raw Score–14)/56 × 100, according to Schechter et al. [19]

Abbreviations: BAI Beck Anxiety Inventory, EWPS Endicott Work Productivity Scale, GAF Global Assessment of Functioning, QIDS-SR Quick Inventory of Depressive Symptomatology-Self Report, Q-LES-Q Quality of Life Measure: Quality of Life, Enjoyment, and Satisfaction Questionnaire—Short Form, SDS Sheehan Disability Scale, WSAS Work and Social Adjustment Scale

Data were collected and analyzed for 319 consecutive outpatients who had a primary DSM-IV diagnosis of MDD and presented for initial outpatient evaluation between 2005 and 2008. Data about prior episodes of MDD and current psychiatric comorbidities were collected along with demographic information.

Clinical measures utilized

The individual item scores were collected at the time of initial assessment for the following as detailed in Table 1:

1. Symptom Severity measures: the Quick Inventory of Depressive Symptomatology-Self Report (QIDS-SR) [13] for depressive symptoms, wherein the severity of MDD depressive symptoms was categorized based on the QIDS-SR scores as detailed by Rush et al. [13]: remission (score 0–5), mild (score 6–10), moderate (score 11–15), severe (score 16–20), or very severe (score > 20). We also used the Beck Anxiety Inventory (BAI) [14] for anxiety symptoms;
2. Functioning measures: Global Assessment of Functioning (GAF) [15], Sheehan Disability Scale (SDS) [16], Work and Social Adjustment Scale (WSAS) [17], and the Endicott Work Productivity Scale (EWPS) [18]; and
3. Quality of Life measure: Quality of Life, Enjoyment, and Satisfaction Questionnaire—Short Form (Q-LES-Q) [18]. This self-report measure contains 16 items, each rated on a 5-point scale (1 = very poor,

2 = poor, 3 = fair, 4 = good, and 5 = very good) during the past week. In the first 14 items, the patient rates his or her satisfaction with physical health, mood, work, household activities, social relationships, family relationships, leisure time activities, ability to function in daily life, sexual drive/interest/performance, economic status, living/housing situation, ability to get around physically, vision, and overall sense of well-being. The total score is calculated and converted to a percentage where 100 would be the best score and 0 is the worst. Q-LES-Q score calculation and interpretation are detailed in Table 1. Q-LES-Q has an internal consistency (Cronbach's alpha) of 0.90 and test-retest reliability (intraclass correlation coefficient) of 0.86 in the community norm sample [19]. Patients with scores less than 10 % of the community norm (mean = 78.3 %, SD = 11.3), that is scores less than 70.5 %, are considered to have quality of life impairments [7, 19]. Patients with scores of 2 or more standard deviations below the community norm, that is scores less than 55.7 %, are considered to have severe impairment in QOL [7].

Data analysis

The raw data were assessed for normality of distribution (Shapiro–Wilk test) and homogeneity of variance (Levene's test). Means and standard deviations were computed for all the measures. A Student's *t* test or an

Table 2 Demographic and clinical characteristics of the study population (total $n = 319$)

Characteristics	Number (%)
Mean age in years (SD)	43.7 (15.5)
Female	221 (67)
Caucasian	219 (69)
African American	47 (15)
Hispanic	21 (7)
Asian	12 (4)
Other	20 (6)
Employed	148 (46)
Primary diagnosis	
Major depression, single episode	74 (23)
Major depression, recurrent	245 (77)
Severity of depressive symptoms ^a	
Remission ^b	15 (5)
Mild	41 (13)
Moderate	101 (32)
Severe	97 (30)
Very severe	64 (20)
Psychiatric comorbidities	156 (49)
Anxiety disorders	93 (29)
Generalized anxiety disorder	39 (12)
Panic disorder	32 (10)
Post-traumatic stress disorder	14 (4)
Obsessive compulsive disorder	3 (1)
Social phobia	1 (<1)
Dysthymic disorder	24 (8)
Personality disorders ^c	21 (7)
Substance abuse/dependence	18 (6)
Drug dependence	10 (3)
Alcohol dependence	5 (2)
Alcohol abuse	2 (1)
Drug abuse	1 (<1)
Eating disorders	6 (2)
Attention deficit hyperactivity disorder	3 (1)
Somatoform disorders	1 (<1)
Impulse-control disorders	1 (<1)

^a Severity levels determined by QIDS-SR cutoff points according to Rush et al. [13], as follows: remission (score 0–5), mild (score 6–10), moderate (score 11–15), severe (score 16–20), or very severe (score > 20)

^b Patients in remission at the time of initial presentation (5 % of the sample) are typically seeking medication maintenance

^c Since the MINI contains a module for antisocial personality disorder only, personality disorders were diagnosed using the DSM-IV criteria and confirmed by consensus

Abbreviations: QIDS-SR Quick Inventory of Depressive Symptomatology-Self Report

analysis of variance (ANOVA) with a Tukey's Studentized Range (HSD) test for multiple comparisons was used to examine differences in the clinical measures across groups.

Pearson's correlation coefficients (r) were employed to determine the correlations between total scores of the Q-LES-Q, QIDS-SR, BAI, GAF, SDS, WSAS, and EWPS. Linear regression analysis was performed to investigate the relationship between QOL, depressive symptom severity, and functioning measures. Forward step-wise selection procedures were used to select the variables with the greatest prognostic value of QOL scores, and only variables with a $p < 0.15$ in univariate analysis were considered for inclusion in the multivariable model. Semi-partial correlation coefficients were calculated to examine how much each factor individually accounted for QOL impairment. All results were considered significant where $p < 0.05$. Statistical analysis was performed using SAS v9.1 computer software package (SAS Institutes Inc., Cary, North Carolina, USA).

Results

The demographic and clinical characteristics of the study population are presented in Table 2. Subjects were predominantly women ($n = 221$, 67 %), Caucasian ($n = 219$, 69 %), and experiencing recurrent MDD ($n = 245$, 77 %) with a mean age of 44 years (SD = 16). Approximately half of the sample subjects were employed ($n = 148$, 46 %), and almost half of the sample had psychiatric comorbid diagnoses ($n = 156$, 49 %).

The mean Q-LES-Q score for this study population was 39.8 % (SD = 16.9), a value presenting greater than two standard deviations below the community norm mean of 78.3 % (SD = 11.3). The mean QIDS-SR was 15.4 (SD = 5.3), indicating a moderate severity level of MDD. The mean scores for the clinical measures appear in Table 3.

Impact of demographic factors on QOL in MDD

No sex differences were noted in any of the measures. However, ethnicity was a significant predictor of Q-LES-Q, QIDS, and SDS scores: these findings were primarily due to the increased levels of symptom severity and functional and QOL impairments reported by Hispanic and Asian subjects. An ANOVA to compare clinical measures across racial groups showed that race was a significant predictor in Q-LES-Q ($p < 0.001$), QIDS ($p = 0.009$), and SDS ($p = 0.039$). A forward step-wise regression of Q-LES-Q scores was performed, and least square means of Q-LES-Q scores by race were generated, revealing that Hispanics have significantly lower Q-LES-Q score than "others" and whites, after adjusting for other covariates. No other significant differences exist between racial categories as detailed in Table 4. In terms of employment status,

Table 3 Assessment scores of study participants, mean (SD)

Assessment	All subjects (<i>n</i> = 319)	Gender		Employment		Depressive Episode		Psychiatric Comorbidities	
		Male (<i>n</i> = 107)	Female (<i>n</i> = 202)	Not working (<i>n</i> = 171)	Working (<i>n</i> = 148)	First (<i>n</i> = 74)	Recurrent (<i>n</i> = 245)	Absent (<i>n</i> = 163)	Present (<i>n</i> = 156)
Q-LES-Q	39.8 (16.9)	38.0 (14.4)	40.8 (18.0)	36.6 (16.7)	43.6 (16.5)	42.4 (18.0)	39.1 (16.6)	39.8 (17.9)	39.9 (15.9)
QIDS-SR	15.4 (5.3)	16.0 (4.5)	15.1 (5.7)	15.9 (5.2)	15.0 (5.4)	14.9 (5.8)	15.6 (5.2)	15.3 (5.3)	15.6 (5.4)
BAI	25.3 (15.0)	23.4 (13.4)	26.3 (15.8)	27.3 (15.5)	23.0 (14.2)	24.1 (15.5)	25.7 (14.9)	24.2 (15.2)	26.5 (14.9)
GAF	54.8 (10.6)	53.9 (11.3)	55.2 (10.3)	52.5 (10.7)	57.3 (10.0)	54.7 (11.0)	54.8 (10.5)	55.4 (9.5)	54.2 (11.5)
SDS	20.8 (7.6)	21.7 (6.8)	20.3 (8.0)	22.4 (7.4)	18.8 (7.4)	20.2 (8.1)	20.9 (7.5)	20.7 (7.6)	20.8 (7.7)
WSAS	24.9 (10.6)	26.3 (9.8)	24.2 (11.0)	26.8 (10.6)	22.8 (10.3)	23.6 (10.8)	25.3 (10.5)	24.3 (10.9)	25.5 (10.3)
EWPS	40.5 (22.9)	40.4 (24.9)	40.6 (21.9)	N/A	40.5 (22.9)	41.7 (25.0)	40.0 (22.0)	39.9 (22.7)	41.2 (23.3)

There were no significant differences between categories of subjects

Abbreviations: BAI Beck Anxiety Inventory, EWPS Endicott Work Productivity Scale, GAF Global Assessment of Functioning, QIDS-SR Quick Inventory of Depressive Symptomatology-Self Report, Q-LES-Q Quality of Life Measure: Quality of Life, Enjoyment, and Satisfaction Questionnaire—Short Form, SDS Sheehan Disability Scale, WSAS Work and Social Adjustment Scale

subjects not currently working were significantly older and had significantly lower/worse Q-LES-Q and GAF scores, with higher/worse BAI, SDS, and WSAS scores as detailed in Table 5.

Impact of clinical characteristics on QOL in MDD

There were no significant differences in any of the symptom severity, functioning, or QOL measures when dichotomized by the presence or absence of psychiatric comorbidities, or by recurrent versus single episode of MDD. As detailed in Table 6, patients with comorbid DSM-IV-diagnosed anxiety disorders had statistically significant higher BAI scores ($p = 0.03$), but did not differ on the rest of the measures. However, when patients were dichotomized employing a BAI score of greater than or equal to 16 (reflecting moderate to severe anxiety according to Beck and Steer [20]) to identify patients with anxious depression [21], increased symptoms of anxiety had a profound negative impact on all of the measures of QOL, functioning, and work productivity.

Impact of depressive symptom severity on QOL

There were statistically significant differences in mean QOL scores between all of the various groups of depression severity, as measured by the QIDS-SR, highlighting the strong association between symptom severity and QOL. The mean Q-LES-Q score for patients in remission was 72.5 (SD = 11.8), as compared to 54.2 (SD = 11.8) in mild, 45.2 (SD = 11.4) in moderate, 34.4 (SD = 12) in severe, and 23.2 (SD = 11.4) in very severe MDD (Table 7). Additionally, BAI scores increased with increased depression symptom severity.

The relationship between symptoms, functioning, and QOL in MDD

Pearson's correlations were calculated to examine the relationships between the symptom measures, measures of functioning and work productivity, and QOL (Table 8). The QIDS-SR, BAI, SDS, and WSAS all were positively correlated with one another (r range, 0.451–0.78). The Q-LES-Q was negatively correlated with all four of these measures (r range, -0.74 to -0.448), an expected and plausible finding. The EWPS was positively correlated with the QIDS-SR, BAI, SDS, and WSAS (r range: 0.38–0.50).

Linear regression analyses were used to further investigate the relationship between Q-LES-Q, demographic variables, clinical measures, and functioning measures. The results are shown in Table 9. In the unadjusted analysis, QIDS-SR, BAI, GAF, SDS, and WSAS were all significant predictors of Q-LES-Q scores ($p < 0.01$ for all). In total, the adjusted regression model describes a significant portion of the variance of Q-LES-Q score (r^2 adj = 0.638). Measures of depressive symptoms severity (QIDS-SR) and measures of functioning/disability were highly predictive of Q-LES-Q scores. QIDS-SR, GAF, and SDS scores accounted for 48.1, 17.4, and 13.3 % (partial correlation values) of the variance in Q-LES-Q, respectively (Table 9).

We also performed an item analysis to determine whether specific aspects of QOL impairment were driving the overall low Q-LES-Q scores for our patients. The overall sample scored the lowest on satisfaction with work, followed by sexual drive, interest, and/or performance. They also scored almost as low on the mood, economic status, and overall well-being items. An item-by-item listing of Q-LES-Q scores from our sample appears in Table 10 alongside the community norm sample [18].

Table 4 Comparison of clinical measures by race, mean (SD)

Race	Q-LES-Q		QIDS-SR		BAI		GAF		SDS		WSAS		EWPS	
	N	Mean	N	Mean	N	Mean	N	Mean	N	Mean	N	Mean	N	Mean
White	219	41.8	218	15.2	218	24.3	196	55.9	215	20.1	218	24.4	113	39.8
Black	47	37.3	47	15.7	46	28.1	44	52.3	46	21.9	47	26.6	19	45.0
Hispanic	21	27.6	21	17.0	21	27.1	20	54.0	20	23.5	20	27.0	6	38.2
Asian	12	26.5	12	19.9	12	29.8	9	47.3	12	25.4	12	28.7	4	44.3
Other	20	45.5	20	13.6	20	24.8	18	53.7	19	19.9	20	22.1	6	40.2

An ANOVA was used to compare clinical measures across racial groups. Race was a significant predictor in Q-LES-Q ($p < 0.001$), QIDS ($p = 0.009$), and SDS ($p = 0.039$). There was no significant difference by race for GAF ($p = 0.055$), BAI ($p = 0.426$), WSAS ($p = 0.259$), or EWPS ($p = 0.911$)

Abbreviations: BAI Beck Anxiety Inventory, EWPS Endicott Work Productivity Scale, GAF Global Assessment of Functioning, QIDS-SR Quick Inventory of Depressive Symptomatology-Self Report, Q-LES-Q Quality of Life Measure: Quality of Life, Enjoyment, and Satisfaction Questionnaire—Short Form, SDS Sheehan Disability Scale, WSAS Work and Social Adjustment Scale

Discussion

This sample of subjects seen in an academic community hospital outpatient program has demographic and clinical characteristics that are typical of what is observed in most outpatient settings [9]. One of the unique features of this clinical sample of patients is the range of severity of depressive symptoms. Some patients were in remission but entered the clinic in order to receive ongoing medication follow-up, while others were un-medicated subjects requesting initial assessment and care. In general, the patients were moderately depressed and had significant functioning impairments as demonstrated by GAF, SDS, and WSAS scores and work productivity impairments as evidenced by EWPS scores. The mean QOL for this clinical sample of 39.8 % on the Q-LES-Q is not only substantially lower than the mean score of 78.3 % (SD = 11.3) for the normal population [7, 19] (where normal limits are within 10 % of community norms, i.e., above 70.5 %), but also represents a value greater than two standard deviations below the community norm mean (i.e., values below 55.7 %) similar to what has been reported in research populations [7]. Our findings are consistent with other studies showing significant impairment of QOL in MDD such as the US STAR*D trial [6], the European FINDER study [22], and another International 6-country study [23]. The mean Q-LES-Q score for our study population is similar to that observed in the STAR*D study [6, 24, 25].

The literature investigating potential sex differences in MDD is quite extensive, but the literature investigating differences in QOL is sparse [26]. We did not find any differences in the measures of QOL, functioning, or symptom severity based on sex. Additionally, when we performed an item-by-item comparison with the Q-LES-Q short form, we observed no statistical or clinically significant differences between women and men.

While we did not find any statistically significant differences in mean outcome measures among genders, we did find some with age and ethnicity. In our clinical sample, older and Hispanic patients had lower QOL ratings, which is consistent with previous studies [6, 24, 25].

In terms of recurrent depression versus first episode, we found that individuals with recurrent depression were less likely to be employed, but did not differ from individuals presenting with their first episode of MDD on depressive symptom severity, level of anxiety, QOL impairment, or any measures of functional impairment. These findings challenge the widely held clinical dictum that the initial episode of depression is less severe, less functionally impairing, and causes less of a detriment to QOL than recurrent illness, suggesting that the actual severity of episodes, measured with a multidimensional approach, is

Table 5 Basic Statistics on Outcome Measures by working status

	N	Mean	Std Dev	Median	Minimum	Maximum
Subjects NOT currently working						
Age	170	46.6	16.8	45.0	18	88
GAF	151	52.5	10.7	51.0	15	75
Q-LES-Q	171	36.6	16.7	35.7	0	88
QIDS-SR	170	15.9	5.2	16.0	3	26
BAI	169	27.3	15.5	27.0	0	63
SDS	167	22.4	7.4	24.0	0	30
WSAS	169	26.8	10.6	29.0	0	40
EWPS	0					
Subjects currently working						
Age	148	40.4	13.1	38.0	18	75
GAF	136	57.3	10.0	60.0	27	85
Q-LES-Q	148	43.6	16.5	42.9	4	91
QIDS-SR	148	15.0	5.4	15.0	2	27
BAI	148	23.0	14.2	22.0	0	59
SDS	145	18.8	7.4	20.0	0	30
WSAS	148	22.8	10.3	25.0	0	40
EWPS	148	40.5	22.9	41.5	0	100

Student's *t* tests were performed on the data presented in Tables 4 and 5. Subjects not currently working were significantly older, had significantly lower GAF and Q-LES-Q scores, with higher BAI, SDS, and WSAS scores ($p < 0.05$ in all cases)

Abbreviations: BAI Beck Anxiety Inventory, EWPS Endicott Work Productivity Scale, GAF Global Assessment of Functioning, QIDS-SR Quick Inventory of Depressive Symptomatology-Self Report, Q-LES-Q Quality of Life Measure: Quality of Life, Enjoyment, and Satisfaction Questionnaire—Short Form, SDS Sheehan Disability Scale, WSAS Work and Social Adjustment Scale

similar for single versus recurrent MDD, while the impact of recurrent episodes in itself may be reflected by the differences in employment rates. Since our sample did include a small percentage of patients who came for an initial evaluation on psychotropic medications or with recent treatment history, it is always possible that these interventions had a mitigating effect on symptom severity, QOL, or functional impairments.

We did not discern a significant difference on QOL measures for individuals presenting with comorbid DSM-IV-diagnosed psychiatric disorders versus those without psychiatric comorbidity, especially with regard to the impact of comorbid anxiety disorders on QOL. Fava et al. [21, 27] have repeatedly reported that depressed patients (and subjects) with higher ratings of anxiety, usually assessed on the anxiety subscale of the Hamilton Rating Scale for Depression, tended to be less responsive to treatment, suggesting a rough treatment ride for those with anxiety present at baseline. The presence of a DSM-IV-diagnosed comorbid anxiety disorder did not impact the scores of Q-LES-Q, QIDS-SR, or WSAS. As expected, individuals with comorbid anxiety disorders did have significantly higher BAI scores than subjects with MDD only. However, when individuals are classified based on the severity of their baseline anxiety into those subjects with “anxious” depression and those without anxious depression, individuals with anxious depression have significantly worse scores on all measures of QOL, symptom severity, and functioning.

Our data demonstrate that impairment in QOL is significantly correlated with impairment in functioning. QOL

Table 6 The Impact of comorbid Anxiety on the measures in MDD, mean (SD)

	DSM-IV-diagnosed anxiety disorder ^a			Anxiety defined by BAI > 16 ^b		
	Absent	Present	<i>p</i>	Absent	Present	<i>p</i>
Q-LES-Q	40.4 (17)	38.5 (16)	0.38	49.5 (17)	35.7 (15)	<0.01
GAF	54.9 (10)	54.6 (12)	0.87	58.6 (8.6)	53.1 (11)	<0.01
QIDS-SR	15.2 (5.4)	16.1 (5.1)	0.15	11.8 (4.8)	17.1 (4.7)	<0.01
BAI	24.1 (15)	28.2 (15)	0.03	8.3 (4.6)	32.8 (12)	<0.01
SDS	20.9 (7.7)	20.4 (7.5)	0.57	16.3 (8.8)	22.6 (6.2)	<0.01
WSAS	24.5 (11)	25.9 (9.9)	0.29	19.4 (12)	27.3 (9.3)	<0.01
EWPS	40.2 (23)	41.3 (24)	0.78	33.5 (22)	44.5 (23)	<0.01

Presence of comorbid anxiety is defined by

^a Anxiety diagnosed as a comorbid Axis I disorder using the MINI

^b BAI score > 16 (according to Beck and Steer [20])

Abbreviations: BAI Beck Anxiety Inventory, EWPS Endicott Work Productivity Scale, GAF Global Assessment of Functioning, QIDS-SR Quick Inventory of Depressive Symptomatology-Self Report, Q-LES-Q Quality of Life Measure: Quality of Life, Enjoyment, and Satisfaction Questionnaire—Short Form, SDS Sheehan Disability Scale, WSAS Work and Social Adjustment Scale

Table 7 Comparison of clinical measures between levels of severity based on QIDS-SR categories, mean (SD)

Depression severity	<i>n</i>	Q-LES-Q	BAI	GAF	SDS	WSAS	<i>n</i>	EWPS
Remission	16	72.5 (11.8) ^a	7.8 (8.3) ^a	66.1 (9.1) ^a	7.0 (5.5) ^a	8.7 (10.9) ^a	9	16.2 (11.4)
Mild	41	54.2 (11.8) ^a	17.4 (14.9) ^b	55.1 (10.7) ^b	15.3 (9.1) ^b	17.8 (12.1) ^b	18	27.7 (14.7)
Moderate	101	45.2 (11.4) ^a	19.9 (11.9) ^b	56.7 (8.7) ^b	19.1 (6.5) ^b	21.8 (8.9) ^b	55	36.7 (22.9) ^b
Severe	97	34.4 (12.0) ^a	27.6 (12.8) ^a	53.3 (10.0) ^b	22.7 (5.3) ^{bc}	27.9 (7.6) ^a	40	47.1 (17.3) ^{bc}
Very severe	64	23.2 (11.4) ^a	39.3 (11.7) ^a	50.6 (11.9) ^b	26.8 (3.8) ^a	33.9 (5.5) ^a	26	55.8 (25.0) ^{bcd}

Groups are significantly different ^a from all other groups, ^b from those in remission, ^c from those with mild MDD, or ^d from those with moderate MDD ($p < 0.05$ in all cases)

Abbreviations: BAI Beck Anxiety Inventory, EWPS Endicott Work Productivity Scale, GAF Global Assessment of Functioning, QIDS-SR Quick Inventory of Depressive Symptomatology-Self Report, Q-LES-Q Quality of Life Measure: Quality of Life, Enjoyment, and Satisfaction Questionnaire—Short Form, SDS Sheehan Disability Scale, WSAS Work and Social Adjustment Scale

Table 8 Pearson's correlation coefficients (*r*) for the assessments of study participants diagnosed with MDD

	Q-LES-Q	QIDS-SR	BAI	GAF	SDS	WSAS	EWPS
Q-LES-Q	1						
QIDS-SR	−0.743	1					
BAI	−0.476	0.555	1				
GAF	0.399	−0.331	−0.201	1			
SDS	−0.664	0.621	0.481	−0.352	1		
WSAS	−0.634	0.621	0.451	−0.299	0.780	1	
EWPS	−0.373	0.500	0.384	−0.145	0.488	0.492	1

For all correlations, $p < 0.01$

Abbreviations: BAI Beck Anxiety Inventory, EWPS Endicott Work Productivity Scale, GAF Global Assessment of Functioning, QIDS-SR Quick Inventory of Depressive Symptomatology-Self Report, Q-LES-Q Quality of Life Measure: Quality of Life, Enjoyment, and Satisfaction Questionnaire—Short Form, SDS Sheehan Disability Scale, WSAS Work and Social Adjustment Scale

Table 9 Results of linear regression analysis of patient variables on Q-LES-Q Scores^a

Variable	Probability value (<i>p</i>)				
	Unadjusted analysis	Adjusted analysis ^b	Coefficient	SE	Partial correlation (r^2)
Age, years	0.82	0.012	−0.102	0.041	0.023
Gender (female)	0.17				
First episode	0.15				
Comorbidities present	0.91				
Employed	<0.001				
QIDS-SR score	<0.001	<0.001	−1.529	0.155	0.481
BAI score	<0.001				
GAF score	<0.001	0.001	0.207	0.062	0.174
SDS score	<0.001	<0.001	−0.494	0.134	0.133
WSAS score	<0.001	0.03	−0.207	0.095	0.021

^a Regression model coefficient of determination: $r_{adj}^2 = 0.638$

^b Adjusted analysis based on forward step-wise variable selection techniques

Abbreviations: BAI Beck Anxiety Inventory, EWPS Endicott Work Productivity Scale, GAF Global Assessment of Functioning, QIDS-SR Quick Inventory of Depressive Symptomatology-Self Report, Q-LES-Q Quality of Life Measure: Quality of Life, Enjoyment, and Satisfaction Questionnaire—Short Form, SDS Sheehan Disability Scale, WSAS Work and Social Adjustment Scale

Table 10 Q-LES-Q item-by-item scores in patients with MDD, mean (SD)

Q-LES-Q item	Community subjects ^a (n = 67)	All CS-PTR subjects (n = 319)	Remission (n = 16)	CS-PTR subject by severity of MDD ^c			
				Mild (n = 41)	Moderate (n = 101)	Severe (n = 97)	Very Severe (n = 64)
1. Physical health	4.3 (0.7)	3.1 (1.1)	4.0 (0.8)	3.7 (0.9)	3.3 (0.9)	3.0 (1.0)	2.4 (1.1)
2. Mood	3.9 (0.9) ^b	2.2 (1.0) ^b	3.9 (0.6)	3.0 (0.8)	2.4 (0.8) ^b	1.8 (0.8) ^b	1.4 (0.6) ^b
3. Work	3.9 (0.9)	2.0 (1.1) ^b	3.7 (1.0) ^b	2.5 (1.3) ^b	2.1 (1.1) ^b	1.8 (0.9) ^b	1.4 (0.8) ^b
4. Household activities	3.8 (0.9)	2.5 (1.0)	3.8 (0.8)	3.2 (1.0)	2.6 (0.9)	2.3 (0.9)	1.8 (0.8)
5. Social relationships	4.1 (0.9)	2.4 (1.1)	3.9 (1.1) ^b	2.9 (1.0) ^b	2.7 (0.9)	2.1 (0.9)	1.9 (0.9)
6. Family relationships	4.2 (0.8)	2.8 (1.2)	3.8 (1.3) ^b	3.0 (1.1)	3.0 (1.1)	2.6 (1.1)	2.4 (1.1)
7. Leisure time activities	4.1 (0.9)	2.3 (1.0)	3.9 (1.0)	3.0 (1.1) ^b	2.5 (0.8)	2.2 (0.9)	1.6 (0.6)
8. Ability to function	4.5 (0.7)	2.6 (1.0)	4.5 (0.6)	3.3 (0.9)	2.7 (0.8)	2.4 (0.8)	1.7 (0.6)
9. Sexual drive	3.9 (1.0)	2.1 (1.1) ^b	2.9 (1.4) ^b	2.4 (1.2) ^b	2.4 (1.2) ^b	2.0 (1.0) ^b	1.6 (0.9) ^b
10. Economic status	3.4 (1.0)	2.2 (1.1) ^b	3.2 (1.2) ^b	2.8 (0.9) ^b	2.4 (1.1) ^b	2.0 (1.0) ^b	1.7 (1.0) ^b
11. Housing	3.9 (0.9)	3.0 (1.1)	3.9 (1.1)	3.6 (0.9)	3.2 (1.1)	2.8 (1.0)	2.3 (1.1)
12. Ability to get around	4.8 (0.5)	3.6 (1.2)	4.6 (0.7)	4.0 (1.0)	3.9 (1.0)	3.4 (1.2)	2.8 (1.2)
13. Vision	4.7 (0.6)	3.3 (1.2)	4.4 (0.8)	4.0 (1.0)	3.6 (1.1)	3.2 (1.2)	2.5 (1.2)
14. Overall sense of well-being	4.3 (0.7)	2.2 (1.0) ^b	4.0 (0.8)	2.8 (1.0)	2.4 (0.8) ^b	1.8 (0.7) ^b	1.5 (0.6) ^b
Q-LES-Q total score	78.3	39.8	72.3	53.9	45	34.6	23.2

^a Community subject scores according to Endicott et al. [18], Rapaport et al. [7], and Schechter et al. [19]

^b Rated as the five lowest scored categories within each group

^c Severity levels determined by QIDS-SR cutoff points according to Rush et al. [13], as follows: remission (score 0–5), mild (score 6–10), moderate (score 11–15), severe (score 16–20), or very severe (score > 20)

Abbreviations: BAI Beck Anxiety Inventory, EWPS Endicott Work Productivity Scale, GAF Global Assessment of Functioning, QIDS-SR Quick Inventory of Depressive Symptomatology-Self Report, Q-LES-Q Quality of Life Measure: Quality of Life, Enjoyment, and Satisfaction Questionnaire—Short Form, MDD major depressive disorder, SDS Sheehan Disability Scale, WSAS Work and Social Adjustment Scale

as measured by the Q-LES-Q is moderately correlated with GAF scores and more highly and inversely correlated with SDS and WSAS scores. Q-LES-Q scores were also inversely correlated with EWPS scores.

In order to fully investigate the relationship between QOL impairment, demographic and clinical variables, and measures of functioning and work productivity, we performed a step-wise linear regression analysis. Our model showed that the QIDS-SR scores (depressive symptom severity) accounted for 48.1 % of the variance in Q-LES-Q scores (QOL), raising doubt that poor QOL in MDD is driven solely by depressive symptom severity. This is consistent with Q-LES-Q studies in research subjects with MDD which showed that illness-specific symptoms account for even less variance in Q-LES-Q scores [7]. Moreover, a number of studies investigated the determinants of QOL for patients with MDD using alternative QOL instruments [28–34]. These studies employed the WHO's Quality of Life Instrument Short Version (WHOQOL-BREF) [35]. The majority of publications report relationships between specific WHOQOL domains and determinants of QOL. Although the amount of variance in specific domains of the WHOQOL-

BREF may vary both based on the specific domain and the specific study, the overall findings suggest that symptom severity, socio-demographic data, self-esteem, response styles, and strength of social network can only account for a small-to-moderate amount of variance in the WHOQOL-BREF and its domain scores [28–30].

The impact of the range of severity of depression on QOL revealed that, as measured by the Q-LES-Q, QOL scores ranged from 72.5 % (SD = 11.8) in patients in remission to 23.2 % (SD = 11.4) in very severe MDD. These data do agree with both the work of Kessler [36] and Maier [37] and suggest that there is a gradient of impairment in QOL that increases with the severity of depressive symptoms, which accounted for 48.1 % of the variance in Q-LES-Q. Moreover, functioning uniquely played a significant role in QOL impairment with the GAF accounting for 17.4 % and the SDS for 13.3 % of the variance in Q-LES-Q.

We also investigated which Q-LES-Q items might be responsible for influencing QOL scores for patients with MDD. For the entire sample, the five items associated with greatest impairment included work, sexual drive, mood, economic status, and overall sense of well-being. These

five items were consistently the items with greatest dysfunction throughout the range of severity of depressive disorder. This is consistent with the items rated lowest from the Rapaport study that included research subjects with MDD [7]. The item-by-item display in Table 10 also shows the wide discrepancy between patients with MDD and the community norm sample scores.

There are always limitations to research performed in clinical settings. This cross-sectional examination of the demographic and clinical characteristics is just a beginning, and we plan to analyze the quarterly data and use these results in future follow-up studies. Another potential criticism of this work is that medical comorbidities were not carefully ascertained for these individuals; we do not know the impact that medical comorbidity may have on our findings. Yet, this is a relatively young sample seeking outpatient psychiatric treatment; hence, it is less likely that this omission was of great significance given this patient population. Although it is true that we did not systematically collect education and socioeconomic data in this study, our clinic cares for a wide range of patients extending from a sliding scale through Medicare to most major insurers, with the majority of subjects having some type of insurance coverage. Other limitations include the possibility that self-reported ratings might differ from clinician-rated measures; however, a significant number of studies demonstrated a high correlation between self-reported and clinician-rated measures. Despite the fact that this sample was drawn from an urban hospital-based psychiatric clinic, the findings could be relevant to patients seen in the inpatient setting, partial hospital setting, or high-end fee-for-service private practice settings as well, given the range of severity, functioning, QOL, diversity of comorbidities, and demographic factors associated with our sample. A final caveat is that we did not include information about the age of onset, total duration of illness, medication, or psychotherapy trials, nor lifetime comorbid psychiatric diagnoses. Inclusion of these variables certainly might have led to a more elegant analysis, but their omission should not adversely skew our data. We believe that a unique aspect of this study lies in the fact that it examines data extracted from a clinical sample with no selection criteria; this more closely mirrors what clinicians typically see in an outpatient practice. Moreover, the detailed data on the 319 MDD patients could enable the readers to compare and contrast the ratings presented in this article with their own patients or research subjects.

Conclusions

This study provides significant details of patient-reported measures of depressive symptoms, anxiety level, functioning, work productivity, and QOL in individuals with

MDD seeking treatment in a typical outpatient setting using measurement-based care. Clinical variables commonly thought to adversely impact QOL and functioning such as recurrence of depression and comorbidity were not associated with greater dysfunction, nor did we observe any gender difference in our findings. Age and ethnicity seem to have an effect on QOL with older and Hispanic individuals having lower QOL. Additionally, both increasing levels of depressive symptom severity and increasing levels of anxiety were associated with poorer QOL, functioning, and work productivity outcomes. In our regression models, depressive symptom severity only accounted for 48.1 % of the variance in QOL. Since the restoration of QOL or overall well-being is the ultimate goal in health care, in general and in MDD in particular [38], it is clear that focusing solely on symptom severity in treating or researching MDD is not sufficient. Our study showed that functioning/disability as measured by the GAF and SDS also accounted for some of the variance in QOL. Additional research should be conducted to identify other contributors to QOL impairment in MDD.

Although further work supporting our findings is necessary, we believe these results demonstrate the need to utilize not only Symptom Severity scales, but also Functioning and Quality of Life measures in major depressive disorder treatment and research.

Acknowledgments The authors would like to thank the Cedars-Sinai Medical Center Psychiatry residents, trainees, staff, and faculty for their exceptional work with patients over the years, and for their contributions in building and maintaining the psychiatric treatment outcome registry cited in this work. The authors would also like to thank Ms. Gitta Morris for her exceptional help during the various stages of development of this manuscript. This research was supported by NARSAD Young Investigator Award Grant#CSMC215387 (Dr. IsHak) and by NIMH Grant#R01MH073765 (Dr. Rapaport, Polier Endowed Chair in Schizophrenia and Related Disorders). Dr. IsHak received research support from NARSAD, Pfizer (ziprasidone monotherapy for major depression). Dr. Rapaport received research support from NIMH and NCCAM, and is an unpaid consultant for Pax Neuroscience.

Conflict of interest Dr. Greenberg, Ms. Bresee, Dr. Balayan, Dr. Fakhry, and Mr. Christensen report no conflict of interest and have no relevant financial disclosure to report.

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