

REVIEW

Quality of Life: The Ultimate Outcome Measure of Interventions in Major Depressive Disorder

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Background: Quality-of-life (QOL) assessment and improvement have recently been recognized as important components of health care, in general, and mental health care, in particular. Patients with major depressive disorder (MDD) have a significantly diminished QOL. **Methods:** Using a Medline search of relevant keywords for the past 26 years, this article reviews the empirical literature to provide information regarding QOL measurement, impairment, impact of comorbidity, and treatment effects in MDD. **Results:** Studies showed that QOL is greatly affected by depression. Severity of depression is also a major contributor to further reduction in QOL when depression is comorbid with other psychiatric and medical disorders. Treatment for MDD has been shown to improve QOL in the acute treatment phase, but QOL remains low compared to healthy controls even when symptoms are in remission following treatment. **Conclusions:** Patients with MDD suffer from poor QOL even after reduction of symptom severity. Clinicians should therefore include QOL assessment as an important part of treating depression. More research is needed to examine the factors contributing to poor QOL in MDD and to develop interventions to ameliorate it. Additionally, future treatment studies of MDD with or without comorbid disorders should track QOL as the ultimate outcome measure of treatment success. (HARV REV PSYCHIATRY 2011;19:229–239.)

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Major Depressive Disorder (MDD) is currently the fourth most disabling disease in the world, causing a significant burden both to individuals and to society. By 2020, MDD is expected to be the second most disabling condition in the world, next to heart disease.¹

Based on general population surveys conducted in many parts of the world, the World Health Organization (WHO) estimated that depression has a lifetime risk of 7%–12% for men and 20%–25% for women.² Data gathered by the Australian Institute of Health and Welfare indicate that everyone at some time in their lives will be affected by depression: their own or someone else's.³ In the United States, the National Comorbidity Survey Replication study revealed that in any given year, 14.8 million adults, or about 6.7% of the population aged 18 and older, suffer from MDD.⁴

MDD has significant morbidity and potential mortality, and leads to disruption in interpersonal relationships, substance abuse, lost work time, and suicide.⁵ Studies also demonstrate that MDD contributes to higher morbidity and mortality in the context of medical illnesses such as myocardial infarction and HIV/AIDS infection.^{6–10} Not surprisingly, successful treatment of depression improves medical

and surgical outcomes.^{11–13} Only in recent years, however, has attention turned to the effect of depression and its treatments on the patient's overall quality of life (QOL). Given the enormous prevalence and burden of depression, as well as the increasing emphasis on wellness as the ultimate goal of medical care, the time is ripe to examine QOL in relation to depression and its treatment.

In 1948, WHO defined health as “a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity.”¹⁴ Ideally, clinical care would need to aim at the restoration of health as demonstrated by a thorough assessment of treatment outcomes. These outcomes would be expected to show a return to the state of health or well-being that could be assessed using QOL metrics. The emergence of measurement-based care has been an important development in this context.¹⁵ QOL improvement and restoration can be considered the ultimate indicator that treatment interventions have succeeded; that is, QOL is the ultimate outcome measure.

This review seeks to address two main questions: (1) What defines QOL, and what metrics are used to measure it in MDD? (2) How is QOL measurement relevant to treatment assessment in MDD, and how could assessing QOL as an outcome measure inform or improve our treatments and practice?

METHODS

We searched MEDLINE and PsycINFO in the last 26 years, from 1984 to 2010. We used the following keywords: major depression OR major depressive disorder OR recurrent depressive disorder OR depressive episode, AND quality of life OR QOL OR health-related quality of life OR HRQOL. We scanned the reference lists of review articles for additional studies. The initial search yielded 591 articles.

Two physicians reviewed the 591 abstracts independently using the following inclusion criteria: (1) articles in English or with available, published English translations, (2) publication in peer-reviewed journals, (2) studies of adult humans, (4) studies (of any design) that focused on MDD (not merely depressive symptoms), and (5) studies that used at least one QOL measure. Both reviewers then independently conducted a literature review using the full-text articles of studies that met the above criteria. The reviewers then reached a consensus about the studies to include in this review.

The study-selection process, described above, yielded 71 articles. Research methodology and key findings were derived from the full text and tables of the selected studies.

WHAT DEFINES QOL AND WHAT METRICS ARE USED TO MEASURE IT IN MDD?

QOL Definition

The literature reveals that there are numerous definitions of QOL. This term is often used interchangeably with functioning, functional impairment, or psychosocial functioning,¹⁶ but it is also sometimes considered a distinct, albeit related, concept. According to WHO, QOL refers to “individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns.”¹⁷ WHO further breaks down this concept into the following essential elements: (1) subjective evaluation, (2) cultural, social, and environmental context, and (3) assessment of specific life domains such as health, work, family and social relations, and leisure activities. By the WHO definition, functioning refers to one's *performance* in activities such as work, love, and play (as rated by self or observers), whereas QOL refers to one's *satisfaction* with the above activities and one's perception of health, among other domains, by self-report.^{18,19}

The issue of subjective versus objective assessment of QOL continues to be debated. Although patient-reported outcomes are starting to take a front seat in modern-day measurement, as evidenced by the National Institutes of Health's Patient-Reported Outcomes Measurement Information System (PROMIS) initiative,^{20,21} those in the medical profession often continue to prefer—and often need—objective measurements as determined by clinicians or third parties. Some authors have argued, however, that QOL is “in the eye of the beholder”²² and therefore would need to be exclusively self-rated.

The relationship of QOL to MDD has not received much attention in the literature. Contrary to some perceptions, depressive symptoms and poor QOL are not synonymous. As stated by da Rocha and colleagues,²³ “Quality of life is neither the opposite of depression, nor is euthymia a synonym of QOL.” In fact, Trompenaars and colleagues²⁴ found that common variance between depressive symptoms and measured QOL did not exceed 25%. While it is not unusual to encounter QOL impairment as a consequence of depression, Moore and colleague²⁵ considered poor QOL as a precursor to depression. Berlim and Fleck²⁶ proposed that an overlap in measuring QOL and depression occurs at three levels: (1) conceptual: depression and QOL represent the same phenomenon; (2) mediational: negative views of self, the world, and hopelessness as conceptualized by Aaron Beck²⁷ could influence reality perception (Aigner and colleagues²⁸ come to a similar conclusion when they posit that poor QOL in depressed patients is due to the influence of mood on QOL

self-ratings); and (3) metric: scales for depression share a number of items with scales for QOL. The same investigators showed in a 12-week study that ratings of QOL improved with improvement of depressive symptoms. The authors wondered, if perceptions of QOL are so influenced by mood, are they synonymous with it? They concluded that depressive symptoms affect the way that patients assess their QOL; that is, it is a mediator variable.

Ritsner and colleagues²⁹ developed the distress/protection vulnerability model of health-related QOL (HRQOL) in severe mental disorders such as schizophrenia. This model, which evolved from the distress/protection model by the same author,³⁰ postulates that QOL is the outcome of the interaction of distress factors and protection factors. The distress factors include low self-esteem, poor coping styles, severity of psychopathology, and personality traits, whereas protection factors include physical health, leisure activities, social relationships, and medications. This model presupposed, and the study results showed, that QOL is more strongly associated with psychosocial factors (such as self-esteem and personality traits) than with disorder-related symptoms. It is therefore not surprising that the authors concluded that treatment needs to focus “not only on simple reduction of symptomatology and/or enhancing levels of functioning, but also on the patient’s subjective well-being and needs”—that is, on QOL.

QOL Measurement

In view of the challenges discussed above, it has been cogently argued that a conceptual or theoretical definition of QOL is needed in order to avoid ongoing controversy and develop operational items to measure QOL.³¹ The work of the World Health Organization Quality of Life Group (WHOQOL) is a good example. The group used the WHO conceptual definition of QOL to operationally define and create a QOL measure known as the WHOQOL-100.³² The newer, abbreviated, more commonly used form is known as the WHOQOL-BREF,³³ which contains 24 items over four domains, enabling subjective rating across cultures: physical health (e.g., mobility), psychological (e.g., self-esteem), social relationships (e.g., social support), and environment (e.g., financial resources).³⁴

Areas covered in QOL assessments typically range from satisfaction with work, relationships, and leisure time, to health, living situation, and overall contentment with one’s life. Corring and Cook³⁵ conducted a study to explore the QOL construct from the perspective of particular consumers—namely, persons with mental illness. The study revealed that patients “simply wish the basics in life” and believe that acquiring them will result in “more satisfactory” QOL. These basics in life included “mental and

physical health, supportive relationships, meaningful occupations, and a positive sense of self.”³⁵

QOL data can be collected through interviews or by using self-report questionnaires, with the latter being more cost-effective. The most commonly referenced instruments in the literature for measuring QOL in MDD are reviewed in Table 1. While a critical comparison of these instruments is beyond the scope of this article, key characteristics of the metrics are detailed.

It is important to consider which aspects of QOL and psychosocial functioning are preferentially measured by different QOL scales. Daly and colleagues⁴⁸ found a low correlation between the abbreviated, 12-item Short-Form Health Survey (SF-12), Work and Social Adjustment Scale (WSAS), and Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q) scores among patients with MDD participating in the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study, and explained this poor overlap by suggesting that each measure emphasizes a different domain of QOL dysfunction, be it psychological, physical, or social. Specifically, the physical domain was found to be emphasized by the SF-12 physical subscale, the psychological domain by the SF-12 mental subscale, and the social domain by the WSAS and Q-LES-Q (which were the two measures with the strongest correlation, with $r = -0.68$). While these results complicate how one interprets the literature relating to QOL in depression, awareness of the results actually allows the measures in question to be used in what Daly and colleagues⁴⁸ describe as a “complementary” fashion: the scales can be used to differentiate among domains of QOL and functioning, and also, when used in conjunction, to assess QOL globally.

QOL ASSESSMENTS AND THE TREATMENT OF MDD

In considering the relevance of QOL measurement in treating depression, it is important to consider some unique implications of QOL improvement in this disease versus others. Improving QOL may itself help to ameliorate depression, whereas, for example, improving QOL is not normally thought to reduce tumor burden, even though the reverse is true. In other words, in a positive feedback loop, treating depression may improve QOL, which, in turn, may protect against future depression. As evidence for this notion, Ezquiaga and colleagues⁴⁹ found that among all the psychosocial variables that they investigated, low QOL in the six months prior to a major depressive episode was the only factor associated with non-complete remission after one year of treatment. By contrast, no significant association was found between remission and clinical variables such as severity of depression.⁴⁹

Table 1. Most Commonly Referenced Measures for Quality of Life in Major Depressive Disorder

| Instrument/reference | Authorship/number of MDD Medline citations | | Description | Administration | Scoring | Reliability/validity | Available languages | Additional notes |
|---|---|---|--|--|---|--|---|------------------|
| | Instrument/reference | Authorship/number of MDD Medline citations | | | | | | |
| Quality of Well-Being (QWB) Scale ³⁶ | Current version by Kaplan & Anderson (original [1973] version by Patrick et al.) 10 MDD references | General HRQOL questionnaire measuring symptoms, mobility, physical activity, & social activity | Interviewer administered; a self-administered version, the QWB-SA, is also available | Weighted scores, with transformation of scores according to a formula Overall score ranges from 0 (nonfunctioning) to 1.0 (optimal functioning) | Reliability: test-retest coefficient for general adult population of 0.96 (consecutive days) ³⁶ Validity: evidence for validity in a variety of diseases, including major depression ³⁶ | English, Spanish, French, Italian, German, and Dutch | May be better suited to policy analysis & economic studies that require calculation of a quality-adjusted life years Authors preferred SF-36 for reviewing a profile of outcomes ³⁶ | |
| EuroQol (EQ-5D) ^{37,38} | Developed in 1990 by the EuroQol Group 23 MDD references | Non-disease-specific instrument for measuring health & HRQOL in patients; includes single-item measures of mobility, self-care, usual activities, pain/discomfort, & anxiety/depression Standardized instrument for measuring health outcome | Self-administered for adults (child-friendly versions in development) Suited for use in postal surveys, in clinics, & face-to-face interviews | Value sets vary for each country | Reliability coefficient of 0.73 (Italian version) Concurrent validity: anxiety & depression domain highly correlated with mental component summary score of the SF-12 ($r = 0.59$) Evidence of construct validity has also been shown ³⁸ | >20 | | |

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Table 1. Most Commonly Referenced Measures for Quality of Life in Major Depressive Disorder (Continued)

| Instrument/reference | Authorship/number of MDD Medline citations | Description | Administration | Scoring | Reliability/validity | Available languages | Additional notes |
|---|--|---|---|---|---|---------------------|---|
| 36-Item Short-Form Health Survey (SF-36) ^{39,40} | Developed in 1992 by the Medical Outcomes Trust, Health Assessment Lab, & Quality Metric Inc. 192 MDD references | Includes one multi-item scale that assesses 8 health concepts: (1) limitations in physical activities because of health problems, (2) limitations in social activities because of physical or emotional problems, (3) limitations in usual role activities because of physical health problems, (4) bodily pain, (5) general mental health (psychological distress & well-being), (6) limitations in usual role activities because of emotional problems, (7) vitality (energy & fatigue), & (8) general health perceptions | Self-administration by persons ≥ 14 years old; may also be administered by a trained interviewer in person or by telephone | Scores range from 0 to 100 All scores above or below 50 can be interpreted, respectively, as above or below the general population norm | Reliability coefficients ranged from 0.65 to 0.94 (median = 0.85) ⁴⁰ Test-retest coefficients of 0.60 to 0.81 (2 weeks), 0.43–0.90 (6 months) ⁴¹ Validity: item-discriminant validity shown to be highly acceptable | >20 | The SF-12 is an abbreviated form of the SF-36 |
| Quality of Life in Depression Scale (QLDS) ^{42,43} | Developed in 1992 by McKenna & Hunt 16 MDD references | 34-item instrument that assesses individuals' ability & capacity to satisfy their daily needs Employs the needs-based model of QOL | Self-administered | Overall score obtained by summing the 34 items; results range from 0 (the highest HRQOL) to 34 (the lowest) | Reliability: internal consistency (Cronbach α) of 0.97 Test-retest coefficient of 0.94 (2 weeks) ⁴² Validity: correlation with General Well-Being Index of 0.79 ³ | >20 | |

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Table 1. Most Commonly Referenced Measures for Quality of Life in Major Depressive Disorder (*Continued*)

| Instrument/reference | Authorship/number of MDD Medline citations | Description | Administration | Scoring | Reliability/validity | Available languages | Additional notes |
|--|---|---|-------------------|--|--|---------------------|---|
| Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q) ⁴⁴ | Created in 1993 by Endicott 16 MDD references | Designed to obtain sensitive information on the degree of enjoyment & satisfaction experienced by patients in various areas of daily functioning Long form includes 60 items & 5 subscales; short form includes 16 items | Self-administered | Raw scores for subscales & total scores are converted to percentage of the maximum total score Higher scores correlate with greater life enjoyment & satisfaction | Reliability coefficient of 0.90–0.96 for subscales; 0.90 for summary scale Test-retest coefficient of 0.63–0.89 for subscales, 0.74 for summary scale (unspecified time) ⁴¹ Validity: correlation of summary scale with Clinical Global Impression scale = –0.62; correlation with Hamilton Rating Scale for Depression = –0.64 Moderate construct validity, with intercorrelations between subscales of 0.41–0.77 ⁴¹ | >20 | Rapaport et al. reported that the community norm ($n = 67$) averaged a score of 83% on the Q-LES-Q, whereas the mean for patients with MDD entering clinical trials ($n = 366$) was 59% ⁴⁵ |
| WHO Quality of Life Assessment Instrument (WHOQOL-100 & WHOQOL-BREF) ^{33,46,47} | Developed in 1996 by the WHO WHOQOL Group 35 MDD references | Generic measure of HRQOL focused around the definition of QOL advocated by WHO; includes the culture & context that influence an individual's perception of health WHOQOL-100 includes 100 items; WHOQOL-BREF includes 24 items; both include 4 domains (physical health, psychological health, social relationships, & environment) | Self-administered | Scores available for domains, facets, & overall Higher scores indicate lower QOL | WHOQOL-100: internal consistency of 0.82–0.95 across domains Test-retest coefficient of 0.83–0.96 (2 weeks) ⁴¹ High construct, convergent, & divergent validity have been shown ⁴⁶ WHOQOL-BREF: internal consistency > 0.8 for all domains (except social relationships, 0.68) Discriminant validity found to be significant for all domains, including psychological ⁴⁷ | >20 | One of the most comprehensive assessments of QOL available; 96% of facets responsive to perceived changes in clinical depression Considered highly sensitive for depression ⁴⁶ |

HRQOL, health-related quality of life; MDD, major depressive disorder; QOL, quality of life; WHO, World Health Organization.

Other studies have investigated the magnitude of QOL impairment in depression and the factors associated with it. Examination of QOL of depressed patients shows that it is significantly lower than that of the healthy population and even than that of individuals with chronic disorders, including hypertension, cancer, and chronic pain.⁵⁰ Saarijarvi and colleagues⁵¹ demonstrated that depression has a substantial negative impact on ability to function and patients' QOL in various ways, including well-being, perceived physical functioning, bodily pain, and general health perceptions. Moreover, QOL in depressed patients seems to be even more negatively affected in the presence of psychiatric and medical comorbid conditions such as posttraumatic stress disorder (PTSD), generalized anxiety disorder, panic disorder,⁵² personality disorders,^{15,49,53,54} substance abuse,⁵⁵ congestive heart failure,⁵⁶ coronary artery disease,^{57,58} diabetes,⁵⁹ chronic obstructive pulmonary disease,⁶⁰ and HIV/AIDS.⁶¹

Several groups have looked at QOL impairment in MDD as compared to other depressive states and other psychiatric pathology. Judd and colleagues⁶² studied functional impairment in patients with MDD and subsyndromal depression, and found that impairments in these two groups are "qualitatively comparable and more similar to each other than they are to any impairment found in subjects without subsyndromal depressive symptoms or major depression." By contrast, in a study of the relationship between mood disorders and QOL, Trompenaars and colleagues²⁴ found that patients with MDD had lower QOL scores than patients with dysthymic disorder or adjustment disorder with depressed mood, and that clinical severity was negatively related to QOL. Comorbid personality disorders also worsened QOL. Rapaport and colleagues⁴⁵ examined QOL impairment in a wider array of psychiatric disorders. They found the following proportions of patients with clinically severe impairment in QOL, defined as two or more standard deviations below the community norm: MDD, 63%; chronic/double depression, 85%; dysthymic disorder, 56%; panic disorder, 20%; obsessive-compulsive disorder, 26%; social phobia, 21%; premenstrual dysphoric disorder, 31%; and PTSD, 59%. Notably, depressive disorders including MDD were associated with the greatest impairment, exceeding that of all anxiety disorders, including PTSD.

A negative correlation between severity of depressive symptoms and QOL was demonstrated in both national and international studies at primary care sites, even in the absence of comorbidities.^{63,64} In order to further examine the relation between depressive symptom severity and QOL, Berlim and colleagues⁶⁵ studied 43 newly diagnosed depressed patients aged 18 to 75 in Brazil. The Beck Depression Inventory (BDI) and the WHOQOL-BREF were utilized to assess patients' symptom severity and QOL. Patients with severe depression (BDI score > 29) experienced significantly worse QOL than patients with mild to moderate

depression. Could clinical or demographic factors be responsible for these poor QOL scores? The same group performed a study of QOL in 140 outpatients with MDD, collecting sociodemographic information such as age, sex, ethnicity, marital status, and education, as well as clinical information such as comorbid psychiatric diagnoses, family history, past history of MDD, suicidality, melancholic features, and psychotic symptoms.⁶⁶ The study concluded that sociodemographic and clinical factors explained only 32.8% of the variance in QOL. Similar findings have been shown in clinical trial subjects with depressive and anxiety disorders using the Q-LES-Q. Rapaport and colleagues⁴⁵ demonstrated substantial impairment in QOL and showed that Q-LES-Q scores are semi-orthogonal to symptoms; symptom severity accounted for a small proportion (e.g., 14% in chronic/double depression) of the variance in QOL scores. Concluding that symptom measurement might not be the most influential factor in determining QOL, the study suggested that QOL should be an additional factor in diagnostic evaluation and treatment planning for these patients.

This suggestion was reaffirmed by the STAR*D study, which explored the sociodemographic and clinical correlates of HRQOL in a large cohort of outpatients with MDD.^{48,67} Even after controlling for age and symptom severity, a number of clinical features and sociodemographic characteristics were independently associated with HRQOL in multiple domains, including age at onset of MDD, ethnicity, marital status, employment status, education level, insurance status, and monthly household income. The results of the analysis highlighted the need to move beyond symptom-based assessment to include QOL assessment.

For the most part, research studies have shown that QOL improves as result of treatment in MDD. These improvements are seen only in the early phases of treatment, however, and—despite remission of depressive symptoms—did not reach QOL ratings observed in the general population.

Research conducted in general practice settings using the WHOQOL-100 has shown that in the first two months following initiation of treatment with antidepressants, QOL significantly improved in 24 out of 25 dimensions such as working capacity, personal relationships, energy and fatigue, and spirituality.⁶⁹ Papakostas and colleagues⁶⁸ reviewed the literature on QOL in MDD, finding that antidepressant treatment could significantly improve QOL measures during the acute phase of treatment. By contrast, impact on QOL was less dramatic during maintenance and continuation phases of treatment.

Shelton and colleagues⁶⁹ conducted a randomized, double-blind, active-control study of sertraline versus venlafaxine XR in MDD. The primary outcome measure was the Q-LES-Q; secondary outcome measures included the 17-item Hamilton Rating Scale for Depression. Participants meeting DSM-IV criteria for MDD were randomly assigned

to eight weeks of double-blind treatment with sertraline ($n = 82$) or venlafaxine XR ($n = 78$). The authors found that both treatments led to significant improvement in depressive symptoms and QOL measures, with no significant differences noted between treatment groups. Due to the relatively short duration of this trial, no predictions could be made about the eventual QOL outcome of this cohort.

In the Factors Influencing Depression Endpoints Research study, Reed and colleagues⁷⁰ studied the QOL outcomes among patients with depression after starting antidepressant treatment. This six-month, European, prospective, observational study was designed to estimate HRQOL in 3468 adult patients with a clinically diagnosed episode of depression, taking measurements at baseline and at three and six months after commencing antidepressant treatment with selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants, and others including herbal remedies, lithium, monoamine oxidase inhibitors, or combinations of antidepressants from more than one of these groups. HRQOL was assessed using the SF-36 and the European Quality of Life-5 Dimensions. Regression analysis identified baseline and treatment variables that were independently and significantly associated with HRQOL outcomes. The study revealed that most HRQOL improvement occurred within three months of starting treatment. It showed that better HRQOL outcomes were strongly associated with fewer somatic symptoms at baseline. Finally, it demonstrated that depression variables (number of previous depressions and current episode duration), as well as somatic symptoms (including pain), were consistently associated with worse HRQOL outcomes.⁷⁰

One noteworthy finding is that patients with depression in remission continue to suffer from QOL impairments. Angermeyer and colleagues⁷¹ studied the QOL among 66 depressed patients after the remission of their depressive episodes. The investigators followed the QOL of patients with Depressive Episode (ICD-10 F32 corresponding to MDD, Single Episode) and Recurrent Depressive Disorder (ICD-10 F33, corresponding to MDD, Recurrent) one, four, and seven months after discharge from hospital. For comparison, a random sample of the general population was also studied. QOL was assessed by means of the WHOQOL-100. The authors found that, shortly after discharge, QOL of patients whose depression remitted was better than that of patients with persisting depression, yet it was still slightly worse than that of the general population. During the subsequent six months, there was no further improvement of QOL. The study concluded that depression implies a persisting impairment of social functioning and living conditions based on both objective (as reported in previous studies) and subjective assessments of QOL.

Little has been done to track, together and over time, changes in depressive symptomatology and variations in QOL. The same study by Angermeyer and colleagues⁷¹ did, however, examine the relationship between clinical changes and self-reported QOL following hospital discharge. The authors distinguished three groups of patients: those whose clinical status remained unchanged over a two-month period following baseline assessment, those whose symptoms improved, and those whose symptoms worsened or recurred. The greatest QOL improvement was seen among those who also improved clinically (although the authors noted that the difference in this QOL change from the clinically static group was not statistically significant). Only slight QOL improvement was seen among the group with stable symptoms; the QOL for these patients remained lower than that of normal controls. All QOL domains except environment declined significantly in the clinically deteriorated group. Thus, a synchronous variability in QOL with clinical symptoms was observed over this relatively brief time frame. It is not until longer-term follow-up results are taken into account, as cited above, that the disconnect between symptom reduction and QOL improvement becomes evident.⁷¹

The above findings imply that symptom-focused treatment can result in the premature impression that the patient has recovered, whereas according to these data, QOL improvement does not generally move in tandem with the resolution of clinically detectable symptoms. If one is assessing only symptom burden, this important distinction between improved symptoms and improved QOL could be overlooked. In essence, effective treatment should lead not only to symptom improvement, but also to restoration of health as evidenced by improved QOL.

The challenge that clinicians therefore continue to face is how to ameliorate QOL impairments beyond remission of depressive symptoms. The reality is that interventions that are designed specifically to improve QOL in MDD have not been systematically investigated. Nevertheless, improved QOL has been observed for psychiatric patients in response to adjunct interventions, including exercise,^{72,73} meditation,⁷⁴ massage,⁷⁵ humor,⁷⁶ cognitive-behavioral therapy,⁷⁷ augmenting agents such as omega-3,⁷⁸ and dopaminergic agents.⁷⁹

CONCLUSIONS AND FUTURE DIRECTIONS

Over the past decade, QOL improvement and wellness have increasingly been emphasized as the ultimate goal of medical care. In a 2004 review of QOL assessments in MDD, Papkostas and colleagues⁶⁸ focused on the impact of MDD treatments on psychosocial functioning and QOL; they emphasized the need for trials involving newer medications and also psychotherapies. In the present review we

examined more closely the theories and metrics of QOL itself as it relates to MDD, and highlighted the various measurement instruments used in the literature relating to QOL in MDD. We have also extended the findings of other reviews—to the effect that QOL improvement lags behind clinical response—by citing previously unreviewed studies; provided evidence that improved QOL may help to prevent relapse of depressive symptoms; and described the importance of QOL assessment in both clinical practice and research. Our further results are as follows:

First, QOL is significantly impaired in MDD. Research has consistently demonstrated that depressed patients' QOL is significantly lower than that of healthy individuals and often even those with chronic medical illness. When depression is comorbid with other medical and psychiatric illnesses, the deterioration in QOL is compounded.

Second, mounting evidence supports the notion that in the clinical context, QOL measurement and improvement—and not merely reduction of depressive symptom—should be integral to treating depression. Of special note here is the finding that good QOL may serve as a protective factor against future depressive episodes. QOL was shown to be a better predictor of sustained remission than was symptom resolution; HRQOL was found to be multidimensional and only partially attributable to clinical variables; and QOL impairments were seen to persist even following successful treatment of depressive symptoms.

Third, more studies are needed to examine the effect of demographic and clinical variables that could account for poor QOL in patients with MDD. Virtually no information is available about the QOL of individuals before the onset of MDD and consequently about the question of whether, and to what degree, poor QOL contributes to the development of MDD. In future research into this important area, and as clinical trials are designed and new instruments developed, we suggest an emphasis not just on symptom severity and functional status, but also on QOL as measured by the patient's self-reported level of satisfaction and perceptions. By the same token, assessments of outcome for MDD treatment—including medication and psychotherapies—need to take into account symptom severity, functioning, and QOL.^{18,19}

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