Factors Associated With Health-Related Quality of Life Among Outpatients With Major Depressive Disorder: A STAR*D Report

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Objective: Major depressive disorder (MDD) is often chronic and is often associated with significant morbidity and mortality. The importance of assessing disability and health-related quality of life (HRQOL) in patients with MDD has only recently been recognized. The aim of this study was to examine sociodemographic and clinical correlates of HRQOL in a large cohort of outpatients with MDD.

Method: Baseline assessments were completed for 1500 consecutive patients enrolled in the Sequenced Treatment Alternatives to Relieve Depression trial, including sociodemographic characteristics and measures of depressive symptom severity, clinical features, and HRQOL. Multiple domains of HRQOL were assessed with the 12-item Short Form Health Survey, the Work and Social Adjustment Scale, and the Quality of Life Enjoyment and Satisfaction Questionnaire. The current analyses were conducted on HRQOL data available for 1397 of the 1500 subjects.

Results: Greater symptom severity was associated with reduced HRQOL by all measures. Even after age and symptom severity were controlled for, 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.

Conclusion: Results strongly suggest the need to assess HRQOL in addition to symptoms in order to gauge the true severity of MDD. This study also highlights the necessity of measuring HRQOL in multiple domains. These results have implications for the assessment of remission and functional recovery in the treatment of MDD.

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Major depressive disorder (MDD) is often chronic or recurrent and is often associated with significant morbidity and mortality. According to the World Health Organization (WHO), MDD is a principal cause of psychosocial dysfunction and an escalating public health problem. Data from the Global Burden of Disease study ranked MDD as the fourth leading cause of disability worldwide in 2000 based on disability-adjusted life-years (DALYs).[1] Furthermore, by 2020, MDD is projected to be the second leading cause of global disability based on DALYs and the foremost cause of disease burden in developed nations.[2] Major depressive disorder also contributes to the development of several chronic medical diseases, including heart disease and diabetes, resulting in further disability, increased health service utilization, and public health burden.[3–5] Additionally, depressive symptoms explain only part of the variability in the functional status of patients with MDD. Patient perceptions of health and functioning are independent determinants of wellness and disease burden,[6–8] yet little attention has been paid to the assessment of health-related quality of life (HRQOL). Patient perceptions of health, psychosocial function, role participation, and life satisfaction are all fundamental components of HRQOL.[9–11]

Clinically significant decrements in areas of HRQOL among patients with MDD[12] are well documented. For instance, the Medical Outcomes Study found that outpatients with MDD reported greater limitations in physical, social, and role functioning (including work, household, and school activities) than persons with many other chronic general medical conditions.[6,13,14] Even outpatients (both primary and specialty care) with symptoms below the threshold for MDD exhibit impaired HRQOL, including perceived physical and mental functioning as measured with the Short Form Health Survey.[6,13,15] Recent studies[16,17] have revealed that patients who achieve full symptom remission do exhibit a return toward premorbid psychosocial function, but patients without remission, even with clinically significant symptom improvement, exhibit persistent impairment in function.

Although depressive symptom severity is a major determinant of HRQOL in MDD, it is only moderately correlated with HRQOL,[18,19] and it is noteworthy that some treatments may enhance HRQOL independent of effect on depressive symptoms.[20] Furthermore, the rates of complete recovery in HRQOL are much lower for patients with chronic MDD or with concurrent comorbid Axis I, II, or III conditions. Also, some effective treatments for depression have not been found to improve HRQOL outcomes,[21] suggesting that improvements in HRQOL may be moderated by clinical, sociodemographic, or biological factors not addressed by standard antidepressant medications used alone.[22–24]

Additionally, correlates of HRQOL may differ across various research settings and patient populations (e.g., primary care vs. specialty care), and some correlates may be unique to particular ethnic or socioeconomic population segments.

HRQOL is a highly relevant clinical outcome that should be aggressively targeted to achieve optimal benefit from the treatment of MDD.[7,25–27] Improved understanding of the association between pretreatment psychosocial functioning, patient clinical features, and sociodemographic characteristics is necessary to optimize long-term outcomes and reduce disability among patients with MDD. Some evidence indicates that measures of HRQOL are predictive of treatment adherence and treatment response.[28,29]

While the measurement of HRQOL requires a range of different types of instruments, few studies of MDD have used such a multidimensional approach as was used in this study. Investigation of baseline characteristics associated with HRQOL of outpatients with MDD should aid in the clinical management of these patients. The current analyses sought to answer the following questions using the baseline data from 1500 participants enrolled in the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study[30,31]:

1. What sociodemographic characteristics are related to HRQOL, including perceived mental and physical function (as measured by the 12-item Short Form Health Survey [SF-12][32]), work and social function (Work and Social Adjustment Scale [WSAS][33]), and satisfaction with life (16-item Quality of Life Enjoyment and Satisfaction Questionnaire [Q-LES-Q][18])?
2. What clinical features of MDD (e.g., symptom severity, course of illness, associated general medical conditions) are related to HRQOL?
3. What sociodemographic and clinical features are independently associated with HRQOL (after controlling for age and depressive symptom severity)?

METHOD

Study Description

The methods of STAR*D are described in more detail elsewhere.[30,31] STAR*D was designed to define prospectively which of several treatments are most effective for outpatients with nonpsychotic MDD who report an unsatisfactory clinical outcome to an initial treatment and, if necessary, subsequent treatment(s). The diagnosis of MDD was established clinically and confirmed with a DSM-IV checklist. Eligible and consenting participants were treated with a selective serotonin reuptake inhibitor (SSRI), after which those with an adequate clinical response could enter a 12-month naturalistic follow-up phase, while those without such a response could enter 1 or more subsequent randomized clinical trials.

Organization of STAR*D

The STAR*D infrastructure included the national coordinating center in Dallas, Tex., the data coordinating center in Pittsburgh, Pa., and 14 regional centers (RCs) across the United States. Each RC oversaw the implementation of the protocol at 2 to 4 clinical sites that provide primary or specialty care in either the public or private sector. In all, nearly half of the sites (19 of 41) were primary care settings.

The clinical research coordinators (CRCs) at each clinical site worked closely with the participants and clinicians, functioned as study coordinators, and provided a liaison between clinical sites and RCs. Research outcomes assessors (ROAs) masked to treatment assignment collected symptom ratings through telephone interviews. Additional research outcomes were collected by an automated interactive voice response (IVR) telephone interview.[34]

Study Participants

Only self-declared outpatients (as opposed to symptomatic volunteers recruited via advertisements) seeking medical care were study eligible. Exclusion criteria were minimal: bipolar disorder, psychotic disorder or symptoms (lifetime), or primary diagnosis of obsessive-compulsive or eating disorder. Only patients with general medical conditions that contraindicated the use of medications used in the first 2 levels of the study and substance dependence requiring inpatient detoxification were excluded. Suicidal patients were eligible, except those requiring immediate hospitalization. Subjects had to be 18 to 75 years of age and could not be pregnant or breastfeeding, or have previously not responded in the current episode to an adequate trial of any treatment used in the first 2 levels of the study. The Institutional Review Boards at the national coordinating, data coordinating, and regional centers and relevant clinical sites, and the Data Safety and Monitoring Board of the National Institute of Mental Health (Bethesda, Md.) approved and monitored the protocol. All subjects signed an informed consent form before being assessed for study entry at the clinical site.

Assessment of Clinical Features and Sociodemographic Characteristics

Baseline measures were collected by CRCs, ROAs, and IVR. They included sociodemographic information, self-reported psychiatric history (including an assessment of suicidality), and severity of depression as assessed by the 17-item Hamilton Rating Scale for Depression (HAM-D-17),[35,36] the 16-item Quick Inventory of Depressive Symptomatology–Clinician-Rated version (QIDS-C-16),[37–40] and the 16-item Quick Inventory of Depressive Symptomatology–Self-Report version (QIDS-SR-16). Depressive symptom severity was also assessed at baseline by telephone interviews with the ROA using the HAM-D-17 and the 30-item Inventory of Depressive Symptomatology–Clinician-Rated Version (IDS-C-30).[39–42]

Health-Related Quality of Life Measures

Many instruments have been developed to quantify HRQOL among patients with depression and other chronic health conditions.[7,11,12,18,43,44] Three distinct measures of HRQOL were selected for use in the STAR*D trial because they assess different domains of HRQOL. The SF-12 (in particular, the perceived physical functioning and mental health functioning subscales),[32] the 16-item Q-LES-Q,[18] and the WSAS[33] were administered using the IVR system. These measures were selected because they assess different domains of HRQOL.

12-item Short Form Health Survey (SF-12). The SF-12 is a self-report measure of perceived health and functioning consisting of 12 questions ranging from general health status to specific physical limitations. Some items are scored as absent/present, while other items are scored on a Likert scale, with varying ranges. Two subscale scores are generated: a physical health factor score and a mental health factor score. Each scale has a possible range from 0 to 100, with a higher score indicating better function in the particular domain. The scales have been constructed so that the population norm for each score is 50. The measure has been shown to be valid and to have acceptable test-retest reliability.[45]

Work and Social Adjustment Scale (WSAS). The WSAS has been used to study the effects of treatment on depression and anxiety. The WSAS is a 5-item self-report scale that assesses the ability to work, to manage affairs at home and socially, and to form and maintain close relationships. Each question is rated on a 0-to-8 Likert scale, with 0 indicating no impairment at all and 8 indicating very severe impairment (range, 0–40). A WSAS score above 20 suggests at least moderately severe functional impairment. Scores between 10 and 20 are associated with significant functional impairment, but less severe clinical symptomatology. The WSAS has demonstrated adequate internal consistency (Cronbach alpha ranges from 0.70 to 0.94) and test-retest reliability ($r = 0.73$). Depressive symptom severity on standardized scales is moderately associated with scores on the WSAS, with significant differences between mildly-to-moderately depressed and moderately-to-severely depressed individuals.[33]

Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q). The Q-LES-Q is a self-report instrument designed to measure satisfaction and enjoyment in various domains of functioning: physical health, feelings, work, household duties, schoolwork/housework, leisure time activities, social relations, and general activities. The short version used in this study has 16 items. The first 14 items ask respondents to assess discrete domains such as social relationships, living or housing situation, and physical health. Item 15 concerns respondents' satisfaction with the medication they are taking, if applicable. Item 16 is a global rating in which respondents are asked to rate their "overall life satisfaction and contentment." Each item is scored on a 5-point Likert scale that indicates the degree of enjoyment or satisfaction achieved during the past week (1 = very poor, 5 = very good). Higher scores represent greater life enjoyment and satisfaction.

Items 1 through 14 of the Q-LES-Q can be summed into a total HRQOL score, and item 16 can be used as a single item measure. For the present analyses, we used only the total score generated by the sum of the first 14 items. This scale has a Cronbach alpha of 0.90 and a test-retest reliability of 0.74 (N = 54). The construct validity of the Q-LES-Q is supported by moderately negative correlations with the Clinical Global Impressions-Severity of Illness scale (CGI-S)[46] and HAM-D-17.

Medical Comorbidity

The current burden due to general medical conditions (GMCs) was assessed by the Cumulative Illness Rating Scale (CIRS).[47,48] The 14-item CIRS, completed by the CRC or clinician using a manual[49] to guide scoring, gauged the severity/morbidity of GMCs relevant to different organ systems. Each condition is scored from 0 (no problem) to 4 (extremely severe/immediate treatment required/end organ failure/severe impairment in function), and then the scores are summed across conditions to generate a total score.

Analytic Approach

The present analyses were derived from baseline assessments of the initial 1397 patients enrolled in the National Institute of Mental Health–funded STAR*D trial. Pearson correlation coefficients were used to estimate the association among the HRQOL measures. All subsequent analyses were conducted separately for each measure of HRQOL. Bivariate analyses between the HRQOL outcomes and clinical and sociodemographic characteristics were assessed using a Pearson correlation coefficient when the clinical features and sociodemographic characteristics were continuous. For binary measures (e.g., gender), a 2-group test was used to compare mean HRQOL scores. For discrete measures with more than 2 levels (e.g., marital status), analyses of variance models were used to compare the HRQOL scores across the groups. If differences were detected, post hoc tests were conducted.

Regression analyses, employing the backward elimination procedure, were used to identify factors independently associated with HRQOL after controlling for the effects of age and depressive symptom severity (as measured by the HAM-D-17 total score obtained by the ROA). In the backward elimination analyses, the F statistics associated with the full set of independent variables are calculated and the variable contributing least to the model is eliminated. This process is repeated until all remaining independent variables are significant at the $p < .10$ level.

We controlled for age and severity of depression because these variables are consistently associated with HRQOL. Since we sought to identify additional factors independent of age and depressive symptom severity, age and severity of depression were forced into each of the regression models. Also, the variables for monthly household income and duration of index episode were transformed (natural logarithm) to meet the assumptions of the models.

As the analyses were exploratory in nature, no correction for multiple tests was made, so results must be interpreted accordingly.

RESULTS

Sample Characteristics

Table 1 summarizes baseline sociodemographic and clinical characteristics of the sample. Of the 1500 participants enrolled in STAR*D, 1397 had complete data for the IVR call, which included the HRQOL assessments. Similar to most samples of outpatients with nonpsychotic MDD in clinical trials, 63% of the participants were female, with a mean ± SD age of 40.6 ± 13.1 years, a mean education of 13.6 years (± 3.2), and a mean yearly household income of $29,724. The yearly household income appears lower than the national average[50] in spite of the inclusion of 28% college graduates in the sample.

The sample consisted of 18% African Americans, 76% white individuals, and 6% individuals of other races. Hispanic ethnicity was reported by 9% of the sample. The ethnic/racial composition of the sample is reflective of the U.S. Census numbers (with the exception of higher representation of African Americans [18% in the study vs. 14% in the U.S. population]).[50] Most subjects were employed, and most had private medical insurance.

The mean ± SD length of illness was 15.8 ± 13.2 years, with a mean age at onset of first major depressive episode (MDE) reported to be at 24.9 ± 13.8 years. Participants had a mean ± SD of 5.7 ± 9.2 MDEs with a mean length of 26.3 ± 60.4 months for the current episode. Interview-administered symptom severity measures indicated that participants presented with moderate severity on both clinician ratings and self-ratings (mean scores: HAM-D-17: 20.5; IDS-C-30: 35.9; QIDS-SR-16: 15.4). Participants endorsed a mean of 3.0 concurrent general medical conditions and demonstrated a mean ± SD CIRS severity index score of 1.2 ± 0.6 and a CIRS total score of 4.3 ± 3.6.

The quality of life and function measures, as assessed by participant calls through the IVR system, revealed a mean ± SD SF-12 mental function score of 26.4 ± 8.4, an SF-12 physical function score of 49.5 ± 11.7, a WSAS score of 23.6 ± 9.2, and a 16-item Q-LES-Q score of 41.8 ± 15.0. The 4 HRQOL measures used in the study have minimal overlap in their assessment of function, quality of life, and satisfaction with life based on the Pearson correlation coefficients (Table 2).

What Sociodemographic Features Are Associated With HRQOL?

Table 3 presents the associations between sociodemographic features and the various domains of HRQOL without adjustments for age or depressive severity.

Table 1. Baseline Characteristics of 1397 Patients With Major Depressive Disorder

Baseline Characteristic	% of Subjects
Gender	
Male	37
Female	63
Race	
White	76
African American	18
Other	6
Hispanic	
Yes	9
No	91
Education	
< High school	11
High school to some post–high school education	61
College graduate+	28
Marital status	
Never married	28
Married/cohabiting	43
Divorced/separated	27
Widowed	3
Employment status	
Employed	59
Unemployed	35
Retired	6
Medical insurance	
Private	57
Public	12
None	32

	Mean (SD)	Median (range)
Age, y	40.6 (13.1)	40 (18–75)
Monthly household income	$2477 ($3005)	$1694 ($0–$30,000)
CIRS severity index score[a]	1.2 (0.6)	1.2 (0–4)
Age at first MDE, y	24.9 (13.8)	21 (2–73)
Length of illness, y	15.8 (13.2)	12 (0–64)
No. of MDEs	5.7 (9.2)	3 (1–98)
Length of current MDE, mo	26.3 (60.4)	7.9 (0–699.3)
Score on quality-of-life measure		
HAM-D-17 (administered by ROA)	20.5 (6.6)	20.5 (0–39)
IDS-C-30 (administered by ROA)	35.9 (11.6)	36 (0–74)
QIDS-SR-16	15.4 (4.2)	15 (2–27)
SF-12		
Physical	49.5 (11.7)	51.9 (16.2–67.5)
Mental	26.4 (8.4)	25.6 (7.4–62.2)
WSAS	23.6 (9.2)	24 (0–40)
Q-LES-Q	41.8 (15.0)	43 (0–95)

[a] The CIRS severity index is used to assess the burden due to general medical conditions.

Abbreviations: CIRS = Cumulative Illness Rating Scale, HAM-D-17 = 17-item Hamilton Rating Scale for Depression, IDS-C-30 = 30-item Inventory of Depressive Symptomatology–Clinician-Rated Version, MDE = major depressive episode, QIDS-SR-16 = 16-item Quick Inventory of Depressive Symptomatology–Self-Report Version, Q-LES-Q = Quality of Life Enjoyment and Satisfaction Questionnaire, ROA = research outcomes assessor, SF-12 = 12-item Short Form Health Survey, WSAS = Work and Social Adjustment Scale.

Table 2. Intercorrelations of Health-Related Quality-of-Life Measures for 1397 Patients With Major Depressive Disorder

Measure	SF-12 Mental	SF-12 Physical	WSAS	Q-LES-Q
SF-12 Mental	1.0	–0.34*	–0.45*	0.4*
SF-12 Physical	–0.34*	1.0	–0.28*	0.36*
WSAS	–0.45*	–0.28*	1.0	–0.69*
Q-LES-Q	0.4*	0.36*	–0.69*	1.0

*p < .0001.

Abbreviations: Q-LES-Q = Quality of Life Enjoyment and Satisfaction Questionnaire, SF-12 = 12-item Short Form Health Survey, WSAS = Work and Social Adjustment Scale.

SF-12 physical function subscale. A significant race effect was detected for self-reported physical function. African Americans reported worse physical function than white individuals (44.9 vs. 50.7; p < .0001). There were significant differences in the mean SF-12 physical function scores across the education categories (p < .0001); better physical function was associated with higher educational attainment. Additionally, there were significant differences in the mean SF-12 physical function scores by employment status (p < .0001), insurance status (p < .0001), and marital status (p < .0001). Retired, as compared to employed, patients reported significantly worse physical function (43.7 vs. 52.4). Patients with public health insurance reported significantly worse physical functioning than those with private health insurance (43.3 vs. 51.7). Widowed patients reported poorer levels of physical function than patients who had never married (43.9 vs. 52.0) (not adjusted for age or depressive severity). Self-reported physical function was not associated with gender or Hispanic ethnicity.

SF-12 mental function subscale. The SF-12 mental function score was not associated with gender or Hispanic ethnicity, but it was significantly associated with race (white individuals functioning worse than African Americans, 26.0 vs. 28.1; p = .0015), medical insurance status, and marital status. There were significant differences in mental function across the employment groups (p < .0001). Retired patients reported the highest mental function, while employed patients reported the lowest mental function (32.2 vs. 25.9). Also, an inverse relation was found between education level and mental function (25.7 for those with at least a college degree vs. 29.3 for those with less than a high school education; i.e., the more highly educated patients reported lower mental function).

WSAS. On the WSAS, a lower score reflects better function and HRQOL. As seen in Table 3, gender, race, and Hispanic ethnicity were not associated with the WSAS scores. However, WSAS score was significantly associated with marital status. Furthermore, there were significant differences in the distribution of WSAS scores across employment categories, with unemployed patients having reported lower HRQOL on this measure as compared with patients who were employed or retired. Similarly, there were significant differences in the distribution of WSAS scores across insurance categories; privately insured patients scored lower (better function) than those with public or no insurance.

Q-LES-Q. As seen in Table 3, satisfaction with life as measured on the Q-LES-Q was not associated with gen-

Table 3. Factors Associated With Health-Related Quality of Life in Patients With Major Depressive Disorder (bivariate analyses)

		SF-12 Physical			SF-12 Mental			WSAS			Q-LES-Q		
Factor	N	Mean	SD	p	Mean	SD	p	Mean	SD	p	Mean	SD	p
Gender				.7636			.0733			.3024			.9869
Male	521	49.7	11.8		26.9	8.6		23.2	9.1		41.8	14.8	
Female	875	49.5	11.7		26.1	8.3		23.8	9.3		41.8	15.2	
Race				< .0001			.0015			.1377			.0631
White	1063	50.7	11.4		26.0	8.2		23.4	9.0		42.2	14.9	
African American	247	44.9	12.1		28.1	8.9		24.6	10.4		39.9	16.2	
Other	84	49.2	11.1		26.8	8.3		22.7	8.1		43.2	11.9	
Hispanic				.3403			.1308			.6956			.4211
Yes	120	48.6	11.3		27.5	9.7		23.3	10.2		40.8	16.7	
No	1275	49.6	11.8		26.3	8.3		23.6	9.1		41.9	14.9	
Education				< .0001			< .0001			.0001			.0001
< High school	150	42.6	11.6		29.3	8.9		25.3	10.1		39.9	15.8	
High school to some post–high school education	853	48.9	11.6		26.2	8.3		24.0	9.4		40.9	15.1	
College graduate+	393	53.5	10.4		25.7	8.3		22.0	8.2		44.5	14.2	
Marital status				< .0001			.0466			.0344			.0120
Never married	386	52.0	10.4		25.5	8.1		23.7	9.0		42.8	14.4	
Married/cohabiting	604	49.6	11.9		26.8	8.4		22.8	9.1		42.6	14.8	
Divorced/separated	370	47.4	12.3		26.4	8.8		24.5	9.5		39.7	15.5	
Widowed	36	43.9	9.5		28.4	8.0		25.1	9.1		40.8	18.3	
Employment status				< .0001			< .0001			< .0001			< .0001
Employed	819	52.4	10.1		25.9	8.3		22.0	8.7		44.3	13.9	
Unemployed	488	45.8	12.6		26.2	8.1		26.4	9.4		37.1	16.0	
Retired	88	43.7	12.2		32.2	9.6		22.6	9.6		44.8	14.3	
Medical insurance				< .0001			0.0136			< .0001			< .0001
Private	765	51.7	10.9		26.6	8.1		22.1	8.8		44.7	13.9	
Public	157	43.3	12.1		27.8	8.3		26.3	9.3		37.2	16.1	
None	425	48.1	12.0		25.6	8.9		25.0	9.5		38.7	15.7	

Abbreviations: Q-LES-Q = Quality of Life Enjoyment and Satisfaction Questionnaire, SF-12 = 12-item Short Form Health Survey, WSAS = Work and Social Adjustment Scale.

der, race, or Hispanic ethnicity. The unemployed, as compared with the employed or retired (p < .0001); those without private insurance, as compared with those with private insurance (p < .0001); and those with less than a college education reported lower levels of satisfaction/ quality of life. Satisfaction with quality of life was only minimally related to marital status (p = .012).

What Clinical Features Are Related to HRQOL?

Table 4 shows that greater depressive symptom severity, as measured by all 3 standardized rating scales (i.e., HAM-D-17, IDS-C-30, and the QIDS-SR-16), was associated (p < .0001) with lower HRQOL in all domains (i.e., SF-12 physical function, SF-12 mental function, WSAS, and Q-LES-Q).

Table 4 also shows that older age, an older age at onset of MDD, longer length of illness, and greater severity of GMCs were all associated with lower HRQOL on the SF-12 physical. In contrast, older age was associated with better mental function (SF-12 mental). Poorer work and social functioning (WSAS) and lower overall life satisfaction (Q-LES-Q) were related to greater severity of medical comorbidity, lower age at onset of MDD, and longer length of depressive illness. However, neither age nor number of prior MDEs was associated with WSAS or Q-LES-Q total scores.

What Sociodemographic and Clinical Features Are Independently Associated With HRQOL (after controlling for age and depressive symptom severity)?

Table 5 presents those factors that were independently associated with the measures of HRQOL after controlling for age and symptom severity (HAM-D-17).

Race, education, medical insurance status, income, severity of general medical comorbidities, and age at onset of first MDE were each significantly and independently associated with physical function (SF-12 physical function subscale). Of note, white patients reported better physical function than African Americans and those of other races. Also, patients with less than a high school education and those with high school to some post–high school education reported poorer physical function than those with at least a college education. As expected, poorer physical function was related to a greater general medical comorbidities burden (CIRS severity index).

SF-12 mental function was related independently to race, education level, employment status, and general medical severity index after controlling for age and depressive symptom severity. Of note, white patients scored significantly lower than both African American patients and those of other races on this measure. Patients with less than a high school education also exhibited higher mental function on the SF-12 compared to patients with at

Table 4. Factors Associated With Health-Related Quality of Life in 1397 Patients With Major Depressive Disorder (continuous variables)

Factor	N[a]	SF-12 Physical		SF-12 Mental		WSAS		Q-LES-Q	
		r	p	*r*	p	*r*	p	*r*	p
Age, y	1395	–0.31	< .0001	0.24	< .0001	–0.01	.7853	0.02	.4527
Monthly household income (log)	1340	0.17	< .0001	0.01	.6316	–0.16	< .0001	0.15	< .0001
CIRS severity index[b]	1397	–0.40	< .0001	0.18	< .0001	0.08	.0032	–0.11	< .0001
Age at onset of first MDE, y	1385	–0.13	< .0001	0.15	< .0001	–0.06	.0184	0.08	.0030
Length of illness, y	1383	–0.17	< .0001	0.08	.0038	0.06	.0308	–0.06	.0183
No. of MDEs	1270	–0.10	.0002	0.05	.0879	0.04	.1223	–0.04	.1301
Length of current MDE, mo (log)	1385	–0.10	.0003	0.00	.9059	0.08	.0018	–0.05	.0572
HAM-D-17 (administered by ROA) score	1370	–0.29	< .0001	–0.33	< .0001	0.48	< .0001	–0.54	< .0001
IDS-C-30 (administered by ROA) score	1372	–0.28	< .0001	–0.39	< .0001	0.54	< .0001	–0.61	< .0001
QIDS-SR-16 (administered by IVR) score	1397	–0.19	< .0001	–0.48	< .0001	0.60	< .0001	–0.65	< .0001

[a] Number of patients with data for this variable.

[b] The CIRS is used to assess the burden due to general medical conditions.

Abbreviations: CIRS = Cumulative Illness Rating Scale, HAM-D-17 = 17-item Hamilton Rating Scale for Depression, IDS-C-30 = 30-item Inventory of Depressive Symptomatology–Clinician-Rated Version, IVR = interactive voice response, MDE = major depressive episode, QIDS-SR-16 = 16-item Quick Inventory of Depressive Symptomatology–Self-Report Version, Q-LES-Q = Quality of Life Enjoyment and Satisfaction Questionnaire, ROA = research outcomes assessor, SF-12 = 12-item Short Form Health Survey, WSAS = Work and Social Adjustment Scale.

least a college education, after controlling for age and severity.

In contrast to the SF-12 findings, WSAS total scores were related only to employment status and household income. Unemployed and retired patients had greater levels of impairment than employed patients.

Life satisfaction (Q-LES-Q) was related independently to marital status, employment status, household income, and age at onset of the first MDE after controlling for age and symptom severity. Specifically, the unemployed reported overall lower life satisfaction than the employed. Also, those who were never married exhibited higher scores (higher satisfaction) than those who were married, independent of the effect of age.

DISCUSSION

This is a preliminary report based on analysis of 1397 depressed outpatients, a subset of the first 1500 enrolled in the large multicenter STAR*D trial who completed the baseline IVR call, including 495 patients from primary care and 902 patients from specialty care. The results from this large sample of patients in both the primary care and specialty care settings clearly demonstrate decrements in multiple domains of HRQOL. Most interestingly, the present study once again indicates that factors in addition to depression severity are related to aspects of HRQOL among outpatients with MDD. The findings also highlight the differential impact of specific sociodemographic and clinical features on several and yet differing domains of perceived impairments in mental and physical function, quality and satisfaction of life, and work and social adjustment.

The contribution of multiple measures of HRQOL toward our understanding of the total nature of impairments in MDD is a unique feature of the results from this study and provides an explanation of why there have been inconsistent findings from previous studies of HRQOL in MDD.

Symptom Severity, Clinical Features, Comorbidity, and Quality of Life

In this sample, severity of depression, no matter what instrument was used, was correlated with all measured domains of HRQOL ($p < .0001$). This is consistent with the extant literature, including findings from the Medical Outcomes Study.[6] Wells and colleagues[6] compared HRQOL of patients with depressive disorders or depressive symptoms and those with hypertension, diabetes, advanced coronary artery disease, angina, arthritis, back problems, lung problems, and gastrointestinal problems. The presence of depressive symptomatology was associated with significantly worse functioning and perceived health as compared with many of these chronic medical conditions.

General medical comorbidities, older age, an older age at onset, and longer length of illness were related to decreased physical functioning and to other measures of HRQOL. These same features, however, may also be associated with better perceived mental functioning. This suggests the possibility that some patients may acclimate to a chronic affective illness. This may also reflect psychometric limitations noted earlier.[21]

Comorbidity of depression with general medical conditions has also been found to produce additive negative effects on HRQOL.[6] Subsequent analyses with the larger full sample will afford the opportunity to test for the effects of these comorbidities independent of the effect identified here. The additive effects of comorbidity on impairments in HRQOL have clear implications for the identification of high-risk patients as well as allocation of resources in order to maximize the assessment and monitoring of HRQOL.

Table 5. Factors Independently Associated With Health-Related Quality-of-Life Measures in 1397 Patients With Major Depressive Disorder (backward, stepwise regression)[a]

Factor	SF-12 Physical, R^2 = .3322			SF-12 Mental, R^2 = .2278			WSAS, R^2 = .2674			Q-LES-Q, R^2 = .3357		
	β	p	sr^2	β	p	sr^2	β	p	sr^2	β	p	sr^2
Age[b]	–0.23	< .0001	0.097	0.09	< .0001	0.05	–0.02	.2934	0.7×10^{-7}	0.03	.3615	0.0004
HAM-D-17 (administered by ROA)[b]	–0.36	< .0001	0.090	–0.49	< .0001	0.110	0.65	< .0001	0.243	–1.19	< .0001	0.301
Race (reference: white)												
African American	–3.41	< .0001	0.026	2.53	< .0001	0.017						
Other	–3.99	.0010	0.004	2.09	.0256	0.003						
Education (reference: college graduate+)												
< High school	–5.44	< .0001	0.018	4.48	< .0001	0.019						
High school to some post–high school education	–2.43	.0003	0.017	1.08	.0368	0.005						
Employment status (reference: employed)												
Unemployed				–0.08	.8702	0.0001	2.82	< .0001	0.024	–3.74	< .0001	0.018
Retired				3.11	.0019	0.006	1.92	.0716	0.003	–1.32	.4323	0.0004
Marital status (reference: married/ cohabiting)												
Never married										2.21	.0233	0.003
Divorced/separated										–0.86	.3571	0.001
Widowed										1.29	.5963	0.00007
Medical insurance (reference: private)												
Public	–3.05	.0019	0.007									
None	–1.20	.0765	0.005									
Monthly household income (log)	0.43	.0007	0.006				–0.24	.0240	0.003	0.44	.0111	0.003
CIRS severity index[c]	–5.08	< .0001	0.055	1.88	< .0001	0.015						
Age at onset of first MDE	0.06	.0133	0.004							0.08	.0113	0.004

[a] For continuous variables, β represents the average increase (or decrease) in the quality-of-life measure associated with a 1-unit increase in the explanatory variable. For discrete variables, β represents the average increase (or decrease) in the quality of life measure for the given level of the explanatory variable relative to the reference group. sr^2 represents squared, semi-partial correlation (the amount of variance of Y explained by X_i controlling for the remaining X_i). $p < .05$ denotes a significant association.

[b] All models forced the inclusion of this variable.

[c] The CIRS is used to assess the burden due to general medical conditions.

Abbreviations: CIRS = Cumulative Illness Rating Scale, HAM-D-17 = 17-item Hamilton Rating Scale for Depression, MDE = major depressive episode, Q-LES-Q = Quality of Life Enjoyment and Satisfaction Questionnaire, ROA = research outcomes assessor, SF-12 = 12-item Short Form Health Survey, WSAS = Work and Social Adjustment Scale.

Sociodemographic Characteristics and Health-Related Quality of Life

Results also indicate that race, education, marital status, and employment status, as well as type of medical insurance coverage, were associated with multiple dimensions of reduced HRQOL among self-identified outpatients with MDD. This is consistent with a number of other studies that have identified associations between sociodemographic factors and HRQOL. In prior research, age, gender,[51,52] occupation, income, education, ethnicity,[53–56] race, and insurance[57] have been found to predict differences in various HRQOL domains. Increasing age has often been associated with decreased HRQOL in the general population,[22,58] while associations between HRQOL outcomes, gender, income, marital status, and education have been shown to vary among different ethnicities and disease groups.[22,24,59]

Wells and Sherbourne[14] speculated that some sociodemographic characteristics, such as race, employment status, or income, could be affected by or causally related to depression. In the present study, these sociodemographic variables were independently associated with HRQOL. Specifically, African American patients reported poorer physical function (SF-12 physical function subscale), yet marginally better mental function (SF-12 mental function subscale) as compared with white patients. It is important to note that Simon et al.[21] have argued that the differential findings in the SF-12 mental function and physical function subscales by race may be an artifact as a result of the use of summary scores generated with items that have reverse loading on the SF-12 mental function and physical function subscales.[21]

Patients with at least a college degree reported the highest physical functioning (SF-12 physical function), work functioning (WSAS), and overall satisfaction (Q-LES-Q), but the lowest mental health functioning (SF-12 mental function). Perhaps educational status is inversely associated with mental health functioning (SF-12 mental function) because patients with higher levels of education are more cognizant of the limitations that depression imposes upon them. In addition, it is possible that greater educational attainment is associated with a more complex and stressful lifestyle or with jobs that require greater cognitive capacity that, in turn, decreases

HRQOL.[60] Highly educated depressed individuals may also have had periods of significantly higher levels of productivity related to mental functioning and may have an awareness of current difficulty achieving prior levels of production.

Unemployed patients reported the lowest overall life satisfaction (Q-LES-Q) and work and social impairment (WSAS); however, these patients reported better physical health than retired patients on the SF-12.

Although we are not aware of any studies on HRQOL of patients with MDD that measured employment status in the same manner as the present study, other researchers have reported an association between financial strain and reduced HRQOL in a range of chronic medical populations[59] as well as greater unemployment among individuals with MDD. Epidemiologic studies have also reported decreased HRQOL among individuals in lower occupational categories.[56,61] Perhaps more closely related to the present research, Simchen et al.[62] found employment status (i.e., full- or part-time employment vs. early pension) significantly associated with reduced mental and physical functioning among patients following coronary bypass surgery.

Finally, patients with private medical insurance reported better physical health and functioning than those with public or no insurance; yet, curiously, patients with no insurance reported better physical functioning than those with public insurance. Perhaps patients who perceive themselves to be in better health may be less motivated to purchase private health insurance or to pursue public insurance. As one would expect, patients with private insurance, however, exhibited better HRQOL on the SF-12 physical health subscale and the Q-LES-Q. A recent population-based study found that health insurance coverage and employment status were each associated with impairments in HRQOL among patients with MDD, even after controlling for a range of other sociodemographic variables.[63]

Thus, the present research indicates that factors other than depression severity contribute significantly to HRQOL among outpatients with MDD. However, specific relationships between different HRQOL measures and sociodemographic characteristics differed depending on the particular HRQOL domain of interest, underscoring the importance of a multidimensional approach to the measurement of HRQOL in MDD. Similar results were obtained with a large population-based study of Asians that found differences in HRQOL outcomes among ethnic groups based on the domain measured.[24]

The present study does have the following limitations: (1) the sample provided HRQOL data from a cross-sectional sample that precludes inferring cause and effect, (2) the study lacked a non-MDD comparison group or a normative community sample, (3) type of employment was not examined in this set of analyses, and (4) results may not generalize to different patient populations (e.g., other types of clinical trials or patients with a different mix of medical comorbidities).

Results of this study of nonpsychotic MDD not only support but extend an emerging body of literature documenting (1) the serious impact of depressive illness on HRQOL and (2) that the degree and nature of these effects are related to multiple baseline clinical and sociodemographic variables. Subsequent analyses will address the nature and timing of improvement in function and quality of life with successful treatment at various levels of the algorithm in STAR*D.

This large study uniquely demonstrates the importance of measurement of multiple domains of HRQOL and provides a rare opportunity to evaluate the effects of ethnic status, socioeconomic characteristics, and clinical setting (primary vs. specialty care), as well as the impact of clinical characteristics on HRQOL. Results highlight the importance of controlling for sociodemographic variables in HRQOL research in patients with MDD and the importance of moving beyond a purely symptoms-based assessment for MDD to include the various domains of HRQOL assessment.

Finally, given the burden of depression and the emphasis on HRQOL, results of this study require replication from other representative clinical as well as epidemiologic studies to evaluate the relationship between sociodemographic, clinical severity, and other illness characteristics and the range of dimensions of HRQOL. Future studies should also address the evaluation of prospective relationships of sociodemographic and clinical features with HRQOL to compare the effects of different treatments and sequences on various domains of HRQOL.

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