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# Quality of Life in Major Depressive Disorder Before/After Multiple Steps of Treatment and One-year Follow-up

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## Abstract

**Objective—**This study examines the impact of Major Depressive Disorder (MDD) and its treatment on Quality of Life (QOL).

**Method—**From the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial, we analyzed complete data of 2,280 adult MDD outpatients at entry/exit of each level of antidepressant treatments and after 12-months of entry to follow-up. QOL was measured using the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q). The proportions of patients scoring 'within-normal' QOL (within 10% of Q-LES-Q community-norms) and those with 'severely-impaired' QOL (>2SD below Q-LES-Q community-norms) were analyzed.

**Results—**Before treatment, no more than 3% of MDD patients experienced 'within-normal' QOL. Following treatment, statistically significant improvements were detected, however the proportion of patients achieving 'within-normal' QOL did not exceed 30%, with>50% of patients experiencing 'severely-impaired' QOL. Although remitted-patients had greater improvements compared to non-remitters, 32%-60% continued to experience reduced QOL. 12-month follow-up data revealed that the proportion of patients experiencing 'within-normal' QOL show a statistically significant decrease in non-remitters.

**Conclusion—**Symptom-focused treatments of MDD may leave a misleading impression that patients have recovered when, in fact, they may be experiencing ongoing QOL deficits. These findings point to the need for investigating specific interventions to ameliorate QOL in MDD.

### Keywords

Quality of Life; Major Depression; Antidepressants; Functional Outcomes; Patient-reported outcomes

## INTRODUCTION

According to the World Health Organization (WHO), quality of life (QOL) represents the individual's subjective evaluation of physical, mental, and social domains (1). Major depressive disorder (MDD), which is the leading cause of disability globally affecting nearly 350 million people worldwide (2), is associated with substantial deficits in QOL (3,4). Importantly, QOL deficits have been shown to persist beyond the clinical resolution of symptoms (5), placing patients at an increased risk for relapse and rising direct and indirect costs (6). A poor QOL often overlaps with depressive symptom severity (7). However, a number of studies have shown that the severity of depressive symptoms explained only a small proportion of the variance in QOL (3, 4, 8). These findings suggest that assessing symptom reduction alone may not be the best way to gauge the success of MDD interventions. Despite being increasingly recognized as an important measure of health in

medical and psychiatric patients (9, 10), QOL needs to be given more attention in clinical and research efforts in MDD.

To fully assess the impact of MDD and its treatment on QOL, we analyzed QOL data from the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial (11, 12), the largest prospective randomized study of treatment effectiveness for outpatients with MDD. Previous STAR*D reports have already shed some light on QOL in MDD (13, 14). Trivedi and colleagues found that greater MDD symptom severity was statistically significantly associated with reduced QOL, and that socio-demographic factors such as race, education, employment, and medical insurance status, as well as general medical and depressive illness were independently associated with poorer QOL (13). Daly and colleagues further examined QOL across psychological, physical, and social domains, showing low correlations between these three domain measures, suggesting that they evaluate different and non-overlapping aspects of function (14). However, the full details of the pre-treatment QOL, the immediate and long-term impact of treatment on QOL, and the clinical significance of the aforementioned themes remain to be investigated. Moreover, studies examining what depressed patients ranked as important goals for treatment revealed that patients hope to return to ‘normal’ levels of functioning and QOL (15). Research seems to point to the notion that patients and clinicians seem to expect this normalization after achieving remission (15), an idea that has yet to be examined. We know very little about the proportions of patients with ‘normal’, i.e., close to community norm QOL scores, before and after treatment. This present analysis examines QOL at entry and exit of each of the four levels of the acute treatment phase as well as the 12-months follow-up phase of the STAR*D study. We hypothesized that:

1. Prior to treatment, MDD patients will report statistically significant QOL deficits, defined as the minority of patients reporting ‘within-normal’ QOL and the majority reporting ‘severely-impaired’ QOL.
2. QOL will show statistically significant improvement with each treatment level, however a proportion of patients will continue to experience the aforementioned QOL deficits immediately after acute treatment.
3. After 12 months, patients who achieved MDD remission will experience higher QOL scores, perhaps close to those seen in community norms.

### Aims of the study

The aim of the study is to examine Quality of Life at the entry and exit of each of the four levels of the acute treatment phase as well as the 12-months follow-up phase of the STAR*D study.

## Material and methods

### Study Population

Funded by the National Institute of Mental health (NIMH), the STAR*D study was conducted at 18 primary care and 23 psychiatric care centers in the United States. STAR*D enrolled 4,041 treatment-seeking outpatients aged 18–75 between 2001 and 2007, all

carrying a primary diagnosis of MDD. Full details of the study's methodology are described elsewhere (11, 12). The authors of the present study obtained an NIMH Data Use Certificate to utilize the STAR*D Public Ver3 dataset. To be eligible for the present analysis, participants needed to have complete data for each of the outcome measures detailed below, at both entry and exit for each level of the study. Patients who were in remission at the beginning of each level were excluded. The analyzed dataset of this study contained 2,280 Level1-participants, 749 Level2-participants, 190 Level3-participants, 56 Level4-participants, and 414 participants from all levels at 12-months follow-up.

## Treatments Administered

The treatment interventions are detailed elsewhere (11, 12). Briefly, treatments were administered according to a fixed-flexible dosing schedule and modified based on each participant's response. Patients were moved to the next level if they did not achieve remission. Participants were enrolled into the following STAR*D levels:

Level 1: Citalopram monotherapy.

Level 2: Switching to sertraline, sustained-release (SR) bupropion, extended-release (XR) venlafaxine, or Cognitive Behavioral Therapy (CBT) OR Augmenting with bupropion SR, buspirone, or CBT.

Level 3: Switching to nortriptyline or mirtazapine OR Augmenting with lithium or Triiodothyronine (T3).

Level 4: Switching to tranylcypromine OR Switching to venlafaxine XR + mirtazapine.

The study used an equipoise stratified randomized design which allowed patients a choice between several switch or augmentation strategies, within the permissible limits of the study design. This approach was adopted in lieu of complete randomization in order to mimic clinical practice (16). During the follow-up phase, patients were strongly advised to continue taking the previously effective drug(s) (17).

## Outcome Measures

QOL was assessed using the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q) (18). The Q-LES-Q is a self-report instrument that measures satisfaction and enjoyment in a series of discrete domains of functioning such as mood, social relationships, living or housing situation, and physical health. This study uses the short version, which has 16 items, each scored on a 5-point Likert scale. Summing up the results of the 14 first items, then dividing by the maximum possible score and multiplying the figure by 100 gives a total score ranging from 0 to 100, with 0 being lowest QOL score and 100 the highest. Community norm samples have a mean Q-LES-Q score of 78.3 (SD=11.3) and scores within 10% of this value, i.e., Q-LES-Q≥70.47, are considered 'within-normal' QOL (1), which corresponds with the 75th percentile. Q-LES-Q scores greater than 2 SD below the community norm scores, i.e., Q-LES-Q scores≤55.7, are considered 'severely-impaired' QOL (19), which corresponds with 95th percentile. The Q-LES-Q has shown moderately negative correlations with the Clinical Global Impressions–Severity of Illness scale (CGI-S) ($r = -0.62$ for the summary scale) and the 17-item Hamilton Rating Scale for Depression ($HRSD_{17}$) ($r = -0.61$ for the summary scale). The Q-LES-Q also has strong psychometric

properties (Cronbach's α=0.90, test-retest reliability r=0.74) (18). Although STAR*D did include the SF-12 as another QOL/Functioning instrument, a number of limitations (with the SF-36 and its abbreviated version, SF-12) precluded its use for our purpose in studying QOL, the most important of which are: the confusion/mix-up in asking patients to self report functioning level in lieu of QOL, and the equal emphasis on physical and mental components of health status (4). Therefore, we limited the analysis to using the Q-LES-Q.

MDD symptom severity was measured using the Quick Inventory of Depressive Symptomatology-Self Report (QIDS-SR) (0 =not depressed to 27=most depressed) with remission is defined as a score≤5 (20). The QIDS-SR is highly correlated with all three versions of the widely utilized clinician-rated Hamilton Rating Scale for Depression, the Montgomery Åsberg Depression Rating Scale, and the Beck Depression Inventory, with a high internal consistency; Cronbach's alpha =0.86 (20).

### Statistical Methods

The variables were assessed and confirmed to have normal distribution. Summary values are expressed as means and standard deviations (SD) for continuous variables, and frequencies (%) for categorical variables. The paired t-test was used for comparisons between entry and exit numerical outcomes, within each level. Effect sizes were calculated for the outcomes (21), in which Cohen's d values of 0.2, 0.5, and 0.8 describe small, medium, and large effects, respectively (22). Since we calculated Cohen's d values in paired samples pre and post treatment, effect sizes were corrected for correlated designs as detailed by Dunlap et al. in 1996 using Equation 3 (23). Entry to exit comparisons of binary variables within each level and follow-up, were assessed using the exact version of the McNemar test for related proportions. The proportions of patients that scored 'within-normal' on the relevant measures were compared between remitters and non-remitters at exit, using the Chi-square test (or Fisher exact test for small sample sizes). Given the number of performed tests, we used a Bonferroni-adjusted 0.01 significance level for each test. Analyses were performed using SAS software, version 9.2 (SAS Institute Inc., Cary, NC).

## RESULTS

### Study Population Demographics

The demographic characteristics of the analyzed patient sample (n=2,280) are shown in Table 1. At baseline, women constituted nearly two thirds of the study population, the majority of patients were Caucasian, more than one half were employed, and about one third were college graduates. The demographic characteristics of the analyzed sample were comparable to those of the whole STAR*D sample.

### Mean Scores on Measures of Depressive Symptom Severity, and Quality of Life

STAR*D level-by-level, pre and post-treatment QOL scores (Q-LES-Q), and depressive symptom severity (QIDS-SR), in addition to scores at entry and exit from the 12-months follow-up phase, are displayed in Table 2.

Patients in the acute treatment phase in each level made statistically significant improvements on both measures. Changes in depressive symptom severity (QIDS-SR scores) showed the following effect sizes (Cohen's *d*) at the end of each level of treatment: *d*=1.05 at Level1, *d*=0.65 at Level2, *d*=0.42 at Level3, and *d*=0.71 at Level4 ($p<0.001$ for all). Changes in QOL, as indicated by differences in pre- and post-treatment scores on the Q-LES-Q, had the following effect sizes: Level1 Cohen's *d*=0.78 ($p<0.001$), Level2 *d*=0.52 ($p<0.001$), Level3 *d*=0.20 ($p=0.002$), and Level4 *d*=0.41 ($p=0.001$).

Interestingly, patients at 12-month follow-up showed statistically significant deterioration on both measures with effects sizes of QIDS-SR Cohen's *d*=-0.43 ($p<0.001$), and Q-LES-Q *d*=-0.38 ($p<0.001$).

It is also important to note that at baseline of Level1, the Pearson's correlation coefficient *(r)* between the QIDS-SR and the Q-LES-Q is 0.74.

## Proportions of Patients with 'Within-normal' Quality of Life Scores

STAR*D level-by-level and 12-months follow-up, entry and exit proportions of patients exhibiting 'within-normal' QOL (Q-LES-Q≥70.47) are displayed in Table 3.

At entry to any level, no more than 3% of MDD patients experienced 'within-normal' QOL. Although treatment increased the number of patients achieving 'within-normal' QOL scores, the majority of patients (70.9%) scored lower than the 'within-normal' QOL range.

Nearly 46.4% of follow-up patients were in remission after 12 months of completing acute treatment. The proportions of follow-up patients experiencing 'within-normal' scores for QOL at 12 months decreased from the time of acute treatment phase completion: from 46.6% to 31.6% ($p<0.001$).

## Proportions of Patients with 'Severely-Impaired' Quality of Life Scores

Level-by-level, pre- and post-treatment in addition to entry and exit follow-up percentages of patients with 'severely-impaired' QOL (two SD below community norms, i.e., Q-LES-Q = <55.7) are displayed in Table 3.

QOL data, at all treatment levels, revealed that the majority (>80%) of MDD patients experienced 'severely-impaired' QOL at entry. The data also shows that treatment statistically significantly decreased the number of patients with 'severely-impaired' QOL at the end of each level. For instance, at the end of Level1, the percentage of patients experiencing 'severely-impaired' QOL decreased from 85.6% to 50.5% ($p<0.001$). However, consistent with the above findings on 'within-normal' scores, sizable proportions of patients were still left with 'severely-impaired' QOL, ranging from 50 to 70%.

The proportions of follow-up patients experiencing 'severely-impaired' QOL showed a statistically significant increase from 28.5% at entry to follow-up, to 42.5% after 12 months ($p<0.001$).

### Proportions of Remitters vs. Non-Remitters with 'Within-Normal' Quality of Life Scores

Remission from MDD is defined as experiencing minimal symptoms or none at all, as measured by QIDS-SR score≤5 (20). As detailed in Table 4, remission was associated with a statistically significant increase in the proportion of patients experiencing 'within-normal' QOL (Q-LES-Q scores) after each level of treatment. However, despite meeting remission criteria, 30–60% of patients did not achieve 'within-normal' QOL scores at exit. Similarly, Table 4 shows that the proportion of patients with 'severely-impaired' QOL showed a statistically significant decrease, especially in remitters. Nevertheless, 9–43% of remitters still scored in the 'severely-impaired' QOL range.

The proportion of follow-up patients with 'severely-impaired' QOL or 'within-normal' QOL scores did not statistically significantly change after 12 months in remitted patients. In contrast, non-remitters showed a statistically significant decrease in proportions of individuals with 'within-normal' QOL scores (from 31.8% to 7.7%; $p<0.001$) and increased proportions of patients with 'severely-impaired' QOL (from 41% to 68%; $p<0.001$).

## DISCUSSION

The present study has a number of important findings: Firstly, MDD patients reported statistically significant QOL deficits, i.e., both high proportions of 'severely-impaired' QOL (i.e. >2SD below community norms), and low proportions of patients scoring within the community norm of QOL scores at the entry of each STAR*D level. Secondly, treatment was associated with statistically significant improvement in QOL, although the majority of all MDD patients continue to experience lower QOL than the general population, with a low proportion of them scoring 'within-normal' QOL; in addition, at each level, patients who achieved remission showed greater improvements in QOL compared to their non-remitting counterparts, yet a sizable proportion of remitted MDD patients did not achieve 'within-normal' QOL scores. Thirdly, follow-up data show that the mean QOL scores of all patients declined after 12 months, as did the proportion of overall patients experiencing 'within-normal' scores; an effect that was only statistically significant in non-remitters.

With no more than 3% of STAR*D entry patients—at any level—reporting 'within-normal' QOL, treating MDD poses a tremendous challenge, not only in treating depressive symptoms but also in ultimately improving QOL. Previous studies have shown that QOL is impaired in MDD and that depression severity is a major contributor to poor QOL (3, 4). It has been postulated that there is a bidirectional relationship between QOL and MDD where MDD could lead to poor QOL and vice versa, in addition to the possible negative influence of depression influence on self evaluation including rating one's own QOL (24–26). Our study shows a strong correlation between the QIDS-SR and the Q-LES-Q of 0.74. In other analyses that examined baseline QOL in MDD data, although moderate to high correlations between depressive symptom severity and QOL were detected, regression analyses showed that the former (as measured by the QIDS-SR) accounted for only 48% of the variance in QOL (as measured by the Q-LES-Q) (4). Reduced QOL in depressed patients may be associated with problems with financial issues, family or social relationships, living situation, or physical health. Earlier pre-treatment analyses of the STAR*D study revealed

that socio-demographically disadvantaged patients with greater general medical and depressive illness burden were at greatest risk for poor QOL (13, 14).

One of the primary objectives of the present study was to determine the extent to which observed deficits in QOL in MDD patients could be improved by treatment, and whether the progress could be maintained at 12 months. Our findings indicate that QOL shows statistical significant improvements when MDD is treated, especially in symptom severity and QOL, with the largest effect sizes observed after the first treatment trial (Level1). However, fewer than 30% of patients exiting Level1 of treatment – both remitters and non-remitters - achieved ‘within-normal’ QOL scores. Additionally, more than 50% of these same patients had ‘severely-impaired’ QOL. Low overall remission rates (e.g. 35% at Level1) may partially explain why most patients continued to experience QOL deficits following treatment.

Our findings reveal that remitted patients showed a remarkable change in the proportions achieving ‘within-normal’ QOL scores after treatment. Of note, 68% of remitted patients at the end of Level 1 treatment reported 'within normal' QOL; a proportion that is not markedly different from the proportion expected for the healthy population. This finding points out to the positive QOL gains that could be made in the early stages of treatment. More strikingly, after 12 months of follow-up, the proportion of patients experiencing ‘within-normal’ QOL scores decreased in non-remitters, a trend not observed in remitters. These findings, coupled with previous studies which had reported that patients who failed to achieve complete symptomatic remission often continued to have psychosocial impairment and were more likely to relapse into full depression (27), reinforce the notion that remission (minimal or no symptoms), as opposed to response (typically 50% reduction in severity), should be one of the primary goals of MDD treatment.

Furthermore, our results suggest that treatment should strive to achieve more than mere symptom resolution or remission. A good proportion of remitted patients still had QOL deficits after treatment. Similar deficits in remitted patients have been reported by Angermeyer and colleagues (5), who stated that remitted patients’ QOL scores remained lower than those observed in non-depressed controls, after seven months following discharge for a depressive episode hospital admission. As some remitted patients may return to a perfectly normal social life, others may experience trouble readjusting to their occupational responsibilities in the wake of their depression. These ongoing deficits imply that remitted patients could remain dissatisfied and feel incapacitated across multiple life domains—even after an otherwise clinically successful treatment regimen.

The expectation that QOL could improve spontaneously after symptom remission was not fully supported by the 12-month follow-up data analysis in this study. On the contrary, QOL suffered from statistically significant deterioration specifically in non-remitters, whereas it did not change from entry to follow-up in patients who maintained remission. The above findings are consistent with the literature on long-term follow-up of QOL in MDD (5, 6).

Evidence suggests that improving QOL is an important treatment target for patients with MDD (25). Zimmerman and colleagues examined the outcomes that patients think are

important when treating their MDD (15). Three factors were found to be better indicators of remission than the mere absence of depressive symptoms: the presence of positive mental health, such as optimism and self-confidence, a return to one's usual, normal self, and a return to normal levels of functioning at home, work, or school (15).

Taken together, the findings suggest that while clinicians should target remission as an initial goal of treatment, they need to subsequently extend their interventions to focus on the specific issues where patients continue to experience difficulty, such as QOL and its domains, notwithstanding the contributing factors highlighted above. Interventions that appear in published original research and/or literature reviews, and are postulated to improve QOL include: cognitive behavioral therapy (28), future-directed therapy (29), combined psychotherapy and pharmacotherapy (30), occupational/vocational therapy (31), dopaminergic agents (32), nutrition and nutritional supplements (33), augmentation with omega-3 (34), exercise (35), meditation and yoga (36), humor (37), massage (38), and music (39). QOL interventions could also include the treatment of possible comorbid medical and psychiatric conditions (40, 41), and treatment of sexual dysfunction (42, 43). However, randomized, controlled, large sample studies need to be conducted to confirm the above interventions' usefulness in MDD. An additional approach to improving QOL consists of identifying and compiling the items poorly rated by patients on baseline QOL measures and utilizing them to guide the creation and implementation of a personalized treatment plan containing interventions to address each impaired domain. A wraparound approach to MDD care, combining the efforts of primary care physicians, specialists, nursing staff, social workers and therapists is an option that could be considered (44). Incorporating QOL measurement and monitoring into clinical practice is becoming a vital component to personalize treatment as detailed above. Newly introduced burden of illness measures incorporating symptom severity, functioning, and QOL, such as the Individual Burden of Illness Index for Depression (IBI-D) (45), represent measurement methodologies that may provide more clinically relevant information.

In summary, increased emphasis should be placed on functional outcomes such as QOL, as important, and perhaps the ultimate, indicators of successful treatment (24–27).

## Limitations and Strengths

Our study has a number of limitations, some are related to the STAR*D study and some are related to our own analysis. The lack of data on patients who dropped out could have potentially provided useful information about their QOL. Younger patients, African-Americans, those with lower education, and individuals with lower income were shown to be more likely to drop out of the STAR*D study (46,47). Medical predictors of attrition included higher side effects and a higher number of Axis I comorbidities. Previous analyses showed that attrition in the first two steps of the STAR*D study was in the vast majority of cases motivated by non-medical reasons; 92% and 90% respectively (47, 48). Attrition makes it difficult to generalize the conclusions from the sample studied. In the future, it would be important to analyze dropout data in order help us better understand the nature of these patients' struggles. The lack of a control group in the STAR*D study, deprived us from useful comparative data. Another limitation involves the challenge of translating the

above research findings into clinical practice. Administering QOL measures, and acting on their findings, must be balanced against the time-constraining realities of modern practice, however QOL improvement is becoming an established treatment goal in many areas of medicine such as ophthalmology (49) and cardiology (50).

The reliance on self-report raises questions about magnification or minimization of ratings, however patient reported outcomes (PRO) using valid and reliable instruments, such as the ones used in STAR*D, is a growing movement in healthcare and is widely supported by NIH PROMIS, WHO, and the FDA PRO initiatives, as well as clinicians and researchers alike. In this analysis we described QOL using both continuous and categorical approaches. A number of authors had criticized categorizing continuous variables (51, 52). We first examined continuous data to detect changes in depressive symptom severity and QOL using statistical significance parameters with effect sizes, and then we examined two categorical variables derived from QOL scores. Although one could never ascertain pre-morbid QOL, we acted on feedback from patients concerning their need for “normalization” of functional outcomes (15). Therefore, we categorized both variables ‘within-normal QOL’ and ‘severely-impaired’ QOL based on parameters identified in previously published research work (3, 19), similar to when depressive symptoms are categorized as “remission” or “response” according to a cutoff score. Another limitation concerns the fact that our study is a post hoc analysis; therefore the study findings should be considered hypothesis-generating and would need to be replicated in prospective randomized placebo-controlled clinical trials. A possible additional limitation of the study concerns the possible paradoxical impact of pharmacological interventions on QOL. Although antidepressants and other drugs are generally safe and well tolerated, the adverse effects associated with medications could negatively impact QOL and thus mitigate their otherwise positive overall effect (53). Additionally, although follow-up patients were strongly encouraged to continue their effective medications, one could not be absolutely sure that the patients completely followed this directive, especially in the absence of medication-level monitoring in this study.

Ethical considerations of clinicians making judgments about patients’ QOL to guide provision of services have long been debated in medicine (54). Moreover, administering questionnaires that might add to the emotional burden of depressed patients recognizing the magnitude of their QOL deficits, have also been debated from an ethical perspective (55).

One of the strengths of the present study is that it distinctly details pre and post-treatment and 12-months follow-up QOL data from a large population of treatment-seeking MDD patients. “Statistically significant" findings, often reported in the literature as indicated by *p* values, which do not adequately inform the reader about the relevance to the findings observed in daily practice or research settings (56), therefore we included the calculation of effect sizes as indicated by Cohen’s *d* (57). An additional strength is the fact that this population of treatment-seeking MDD patients, recruited from primary care and psychiatry specialty clinics, is representative of what clinicians see in outpatient settings. The findings can be extrapolated to everyday practice, with the one caveat that the majority of patients are Caucasians, which limits the applicability of this analysis to ethnic groups such as African-American, Hispanic, Asian, or Native-American patients. Future research effort to study QOL in minority groups is critically needed.

## CONCLUSION

The present analysis highlights the major pitfalls associated with MDD treatments that are purely symptom-focused. Such treatments can give the misleading impression that a patient has recovered, when in fact the patient continues to experience ongoing deficits in QOL. QOL did not improve further after the acute treatment phase even in remitters, and non-remitters showed a statistically significant decline at follow-up after one year. Consequently, clinicians and researchers need to move beyond the mere assessment of symptoms when treating and/or researching MDD, by incorporating QOL measurement, and by investigating specific and personalized interventions to ameliorate QOL.

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**Significant Outcomes**

- An analysis of 2,280 adult Major depressive disorder patients showed extensive and statistically significant decreased quality of life prior to treatment.
- Treatment had a statistically significant positive impact on quality of life. Nevertheless a majority of patients continue to experience quality of life deficits
- Quality of life scores declined after 12 months, as did the proportion of overall patients experiencing ‘within-normal’ scores.

**Limitations**

- The study lacked a placebo arm, and this post hoc analysis relied on self-reported outcomes.
- Possible paradoxical impact of pharmacological interventions on quality of life cannot be excluded.

## Table 1

Demographic and Baseline Characteristics of the STAR*D Analyzed Sample with Major Depressive Disorder (MDD)

| **STAR*D Subjects with Complete QOL and Symptom Severity Data Number of Subjects=2,280** | |
|---|---|
| Age range | 18.1 – 75.6 |
| **Demographics: n (%)** | |
| | 2,280 (100%) |
| Mean Age (SD) | 42.6 (13.0) |
| Female | 1,432 (62.8%) |
| Caucasian | 1,846 (80.9%) |
| Hispanic | 239 (10.5%) |
| College Graduate | 686 (30.1%) |
| Employed | 1301 (57.1%) |
| Living with Spouse/Partner | 1046 (45.9%) |
| **Baseline Measures: Mean (SD)** | |
| QOL (Q-LES-Q) | 41.5 (14.2) |
| MDD Symptom Severity (QIDS-SR) | 15.4 (5.0) |

**Abbreviations**

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

**Table 2**

Mean and SD of Measures of depressive symptom severity (QIDS-SR), and quality of life (Q-LES-Q), with Mean (SD) of Change, and Effect Sizes or ES (Dunlap corrected)

| Level* | *N* | QIDS-SR | | | | Q-LES-Q | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Entry Mean (SD) | Exit Mean (SD) | Change Mean (SD) | *p* (ES) | Entry Mean (SD) | Exit Mean (SD) | Change Mean (SD) | *p* (ES) |
| 1 | 2,280 | 15.4 (4.8) | 9.5 (6.5) | −6.1 (6.5) | < 0.001 (1.05) | 41.5 (14.2) | 56.6 (21.9) | 15.1 (19.4) | < 0.001 (0.78) |
| 2 | 749 | 14.3 (4.7) | 10.5 (6.5) | −3.8 (5.8) | < 0.001 (0.65) | 42.1 (15.5) | 51.5 (20.1) | 9.5 (17.5) | 0.001 (0.52) |
| 3 | 190 | 15.5 (4.8) | 13.1 (6.3) | −2.4 (5.6) | < 0.001 (0.42) | 38.8 (14.7) | 42.2 (18.1) | 3.4 (15.2) | 0.002 (0.20) |
| 4 | 56 | 16.4 (4.6) | 12.3 (6.5) | −4.1 (6.3) | < 0.001 (0.71) | 36.8 (14.3) | 44.0 (19.4) | 7.2 (15.6) | 0.001 (0.41) |
| 12-m. f/u | 414 | 5.6 (3.7) | 7.7 (5.7) | 2.2 (5.1) | < 0.001 (0.43) | 67.1 (17.8) | 59.7 (20.6) | −7.4 (16.1) | < 0.001 (−0.38) |

P values are considered significant at 0.01 or less (Bonferroni-adjusted), Effect sizes are Dunlap corrected for correlated designs (Dunlap et al., 1996).

*Values compared between entry and exit at each level and between entry to follow-up and exit at 12 months of f/u.

STAR*D Levels:
Level 1: Citalopram monotherapy
Level 2: Switching to sertraline, bupropion SR, venlafaxine XR, or CBT OR Augmenting with bupropion SR, buspirone, or CBT
Level 3: Switching to nortriptyline or mirtazapine OR Augmenting with lithium or T3
Level 4: Switching to tranylcypromine OR Switching to venlafaxine XR + mirtazapine

**Abbreviations:** 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

**Table 3**

Proportions of Patients scoring at 'Within-Normal' and 'Severely-Impaired' Quality of Life at Entry and Exit from each Level and F/U.

| Level* | *N* | 'Within-Normal QOL' | | | 'Severely Impaired' QOL | | |
|---|---|---|---|---|---|---|---|
| | | Entry (%) | Exit (%) | McNemar Tes *p* value | Entry (%) | Exit (%) | McNemar Test *p* value |
| 1 | 2,280 | 1.7 | 29.1 | < 0.001 | 85.6 | 50.5 | < 0.001 |
| 2 | 749 | 2.9 | 19.5 | < 0.001 | 83.3 | 59.5 | < 0.001 |
| 3 | 190 | 1.6 | 7.9 | 0.008 | 89.5 | 81.1 | 0.023 |
| 4 | 56 | 1.8 | 8.9 | 0.220 | 91.1 | 69.6 | 0.004 |
| 12-m. f/u | 414 | 46.6 | 31.6 | < 0.001 | 28.5 | 42.5 | < 0.001 |

P values are considered significant at 0.01 or less (Bonferroni-adjusted).

*Values compared between entry and exit at each level and between entry to follow-up and exit at 12 months of f/u.

QOL 'Within-Normal' is defined as Q-LES-Q scores within 10% of community norms. Since community norm samples have an average Q-LES-Q of 78.3 (SD=11.3), a Q-LES-Q>=70.47 is considered 'within-normal' (Endicott et al., 1993, Rapaport et al., 2005, and Schechter et al., 2007). Severe Impairment in QOL is defined as Q-LES-Q scores greater than 2 SD below the community norms. Since community norm samples have an average Q-LES-Q of 78.3 (SD=11.3), a Q-LES-Q=<55.7 is considered 'severely-impaired' (Endicott et al., 1993, Rapaport et al., 2005, and Schechter et al., 2007).

STAR*D Levels:
Level 1: Citalopram monotherapy
Level 2: Switching to sertraline, bupropion SR, venlafaxine XR, or CBT OR Augmenting with bupropion SR, buspirone, or CBT
Level 3: Switching to nortriptyline or mirtazapine OR Augmenting with lithium or T3
Level 4: Switching to tranylcypromine OR Switching to venlafaxine XR + mirtazapine

**Abbreviations:** Q-LES-Q = Quality of Life measure: Quality of Life, Enjoyment, and Satisfaction Questionnaire – Short Form

## Table 4

Proportions of Remitters/Non-Remitters at 'Within-Normal and 'Severely Impaired' Quality of Life at Entry/Exit from each Level and Follow-up.

| | Remitters | | | | Non-Remitters | | | | Difference at Exit |
|---|---|---|---|---|---|---|---|---|---|
| **Level** | ***N*** | **'Within-Normal' QOL Entry (%)** | **'Within-Normal' QOL Exit (%)** | **McNemar Test *p* value** | ***N*** | **'Within-Normal' QOL Entry (%)** | **'Within-Normal' QOL Exit (%)** | **McNemar Test *p* value** | **Chi-Square or Fisher Test p value** |
| 1 | 812 | 3.0 | 68.0 | < 0.001 | 1,468 | 1.0 | 7.6 | < 0.001 | < 0.001 |
| 2 | 208 | 5.8 | 52.4 | < 0.001 | 541 | 1.8 | 6.8 | < 0.001 | < 0.001 |
| 3 | 30 | 0 | 40.0 | < 0.001 | 160 | 1.9 | 1.9 | n/a | < 0.001* |
| 4 | 8 | 0 | 25.0 | 0.500 | 48 | 2.1 | 6.3 | 0.630 | 0.144* |
| 12-mo. f/u | 193 | 63.4 | 58.8 | 0.260 | 221 | 31.8 | 7.7 | < 0.001 | < 0.001 |
| **Level** | ***N*** | **'Severely-Impaired' QOL Base (%)** | **'Severely-Impaired' QOL Exit (%)** | **McNemar Test *p* value** | ***N*** | **'Severely-Impaired' QOL Base (%)** | **'Severely-Impaired' QOL Exit (%)** | **McNemar Test *p* value** | **Chi-Square or Fisher Test p value** |
| 1 | 812 | 79.3 | 9.0 | < 0.001 | 1,468 | 89.0 | 73.4 | < 0.001 | < 0.001 |
| 2 | 208 | 74.5 | 16.3 | < 0.001 | 541 | 86.7 | 76.2 | < 0.001 | < 0.001 |
| 3 | 30 | 83.3 | 43.3 | 0.004 | 160 | 90.6 | 88.1 | 0.570 | < 0.001* |
| 4 | 8 | 87.5 | 25 | 0.063 | 48 | 91.7 | 77.1 | 0.065 | 0.007* |
| 12-mo. f/u | 193 | 14.4 | 13.4 | 0.860 | 221 | 40.9 | 68.2 | < 0.001 | < 0.001 |

P values are considered significant at 0.01 or less (Bonferroni-adjusted).

*Fisher exact test used due to small sample size

QOL 'Within-Normal' is defined as Q-LES-Q scores within 10% of community norms. Since community norm samples have an average Q-LES-Q of 78.3 (SD=11.3), a Q-LES-Q>=70.47 is considered 'within-normal' (Endicott et al., 1993, Rapaport et al., 2005, and Schechter et al., 2007). Severe Impairment in QOL is defined as Q-LES-Q scores greater than 2 SD below the community norms. Since community norm samples have an average Q-LES-Q of 78.3 (SD=11.3), a Q-LES-Q=<55.7 is considered 'severely-impaired' (Endicott et al., 1993, Rapaport et al., 2005, and Schechter et al., 2007).

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Level 3: Switching to nortriptyline or mirtazapine OR Augmenting with lithium or T3
Level 4: Switching to tranylcypromine OR Switching to venlafaxine XR + mirtazapine

**Abbreviations:** f/u = Follow-up; Q-LES-Q = Quality of Life measure: Quality of Life, Enjoyment, and Satisfaction Questionnaire – Short Form