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# Quality of Life and Perceived Cognitive Dysfunction in Patients with Major Depressive Disorder: A Longitudinal Observational Study

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# Quality of Life and Perceived Cognitive Dysfunction in Patients with Major Depressive Disorder: A Longitudinal Observational Study


## Abstract

### Background

Major Depressive Disorder (MDD) is recognized as one of the most prevalent public health disorders globally associated with increased rates of mortality, morbidity and disability. Numerous research has yielded inconclusive findings about the impact of depression treatment on quality of life (QOL).

### Aim

To evaluate the severity of depression symptoms and their relationship to QOL and perceived cognitive dysfunction in Jordanian patients diagnosed with MDD.

### Method

The study included patients from both genders, between 18-65 years old, and diagnosed with MDD. They attended two visits with 6-week interval period and completed three self- administered questionnaires in both visits: a 9-item Patient Health Questionnaire (PHQ-9) assesses depression severity, patient-rated Perceived Deficit Questionnaire (PDQ-5) assesses cognitive function, and World Health Organization Quality of Life Brief (WHOQOL-BREF) format for assessing the quality of life and health satisfaction.

### Results

A total of 112 patients were included in the study. Twenty patients withdrew their consent to participate therefore only 92 patients (34 males and 58 females) completed both sets of questionnaires. Significant reductions were found in the scores (mean ±SD) for PHQ-9 before and after treatment (19±5.4 and 7.1±5.1, respectively, $P<0.0001$), and PDQ-5 (13±4.4 and 7.2±4, respectively, $P<0.0001$).

Scores for WHOQOL-BREF were significantly increased in several domains. Significant correlations were found between the scores of all the dimensions for WHOQOL-BREF and PDQ-5 but inverse correlation was found between total scores for PHQ-9 and PDQ-5.

**Conclusion**

Patients with MDD showed significant improvement in their depression symptoms, cognition and QOL after treatment. Depression severity showed significant positive correlation with QOL and inverse correlation with cognition in these patients.

**Keywords**

MDD, QOL, questionnaire, cognition, Antidepressants, DSM-5

## Introduction

The fifth edition of Diagnostic and Statistical Manual of Mental Disorders (DSM-5) diagnostic criteria identifies cognitive deficits as a core symptom of depression, including difficulty thinking, concentrating, and/or making decisions (1,2). Major Depressive Disorder (MDD) is recognized as one of the most common public health disorders worldwide, that is associated with high mortality, morbidity and disability (3).

Patients with MDD have a significantly poor quality of life (QOL) that leads to high rate of relapse and increases the overall related cost (3,4). Depression severity is statistically significantly correlated with impaired QOL, however, QOL changes are not fully paralleled by changes in depression (3,5).

Several studies have demonstrated the effects of treatments for depression on QOL and found mixed results (5). Some studies have found that treatment of depression significantly improves the QOL (6,7), whereas other studies have found no major improvement in the QOL (3,4,8,9). In order to reach the optimum long-term outcomes in patients with depression, improving QOL in these patients is crucial

(10). Therefore, it is mandatory to assess whether current treatments for depression significantly improve QOL.

Cognitive deficit is common and persistent in patients with MDD and it's recognized as one of the predominant symptoms of this disease (11,12). It occurs in several domains including memory, attention/concentration, processing psychomotor speed and executive functions (problem solving, decision making, and judgment) (13,14). Cognitive deficit has been associated with impairment in psychosocial function, worse work productivity, poor quality of life and increased relapse in patients with MDD (1,12,13,15). Meta-analysis has been conducted in MDD patients to examine the effects of pharmacotherapy on cognitive dysfunctions and have been found different results (13). Some studies have reported that cognitive function improved with treatment whereas others have found no change in the performance of many cognitive functions (13).

To our knowledge, there have neither been studies to discuss cognitive functions nor the association of both QOL and cognitive impairment in patients with MDD in Jordan. Therefore, the evaluation of cognitive function and QOL in patients with MDD is necessary to optimize the outcome in these patients.

The aim of the current study is to evaluate the severity of depression symptoms and their relationship to QOL and perceived cognitive dysfunction in patients diagnosed with MDD in Jordan.

# Methods

### Study Design and Setting

This was an observational longitudinal study conducted in a private outpatient psychiatric clinic in Amman, Jordan. The study commenced in early 2022 and was completed in September 2023. The study evaluated depressive symptoms, perceived cognitive dysfunction, and quality of life

at baseline, six weeks after treatment initiation, and, where follow-up data were available, one year after baseline.

## Participants and Eligibility Criteria

Eligible participants were adults aged 18–65 years, of either sex, diagnosed with MDD according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). Patients with psychotic symptoms or uncontrolled chronic medical illnesses were excluded. The Methods section of the source manuscript reports that 112 patients were eligible and that 92 provided informed consent and were included in the main analysis. Participants provided sociodemographic and clinical information, including age, sex, educational attainment, medical history, history and duration of depressive episodes, and treatment received.

## Assessment and Follow-up

Participants were assessed at baseline before treatment and six weeks after treatment initiation. A one-year follow-up assessment was available for 49 participants; the remaining participants were not assessed at that time point. At each assessment, participants completed three self-administered questionnaires: the Patient Health Questionnaire-9 (PHQ-9), the instrument identified as the Patient-rated Perceived Deficit Questionnaire (PDQ-5) in the source manuscript, and the World Health Organization Quality of Life-BREF (WHOQOL-BREF).

## Depressive Symptom Severity

Depressive symptoms were assessed using the nine-item Patient Health Questionnaire (PHQ-9), with total scores ranging from 0 to 27; higher scores indicate greater symptom severity (11) The source manuscript reports these categories: mild, 5–9; moderate, 10–14; moderately severe, 15–19; and severe, 20–27.

### Perceived Cognitive Dysfunction

Perceived cognitive dysfunction was assessed using the Patient-rated Perceived Deficits Questionnaire (PDQ-5), a tool for measuring subjective cognitive function. It consisted of five items, each rated on a five-point scale from 0 (never) to 4 (almost always), covering attention/concentration, retrospective memory, prospective memory, planning/organization, and perceived cognitive lapses (11,12). A cutoff score of 12 or higher was used to estimate cognitive impairment.

### Quality of Life

Quality of life was assessed using the 26-item World Health Organization Quality of Life-BREF (WHOQOL-BREF), an abbreviated version of the WHOQOL-100(16). The instrument includes items covering overall quality of life and general health, and is scored across four domains: physical health, psychological health, social relationships, and environment (4).

### Statistical analysis

Data was analyzed using GraphPad Prism 7 (GraphPad Software Inc., La Jolla, CA, USA). Continuous variables were summarized as means and standard deviations (SD). The Mann–Whitney test was used to compare questionnaire scores before and after treatment when the data were non-parametric. Spearman correlation analysis was used to assess associations among quality of life, depressive symptom severity, and perceived cognitive dysfunction. Statistical significance was set at ($P < 0.05$).

## Results

### Participant Characteristics

A total of 92 patients were included in the main analysis. The mean age was 32.7 ± 11.0 years, and the sample comprised 34 males (37.0%) and 58 females (63.0%). Regarding educational attainment, 78 participants had university education and 14 had completed high school. Forty-two participants

(45.7%) were single, 45 (48.9%) were married, and five (5.4%) were divorced or separated. Fifty-six participants (60.9%) were reported to have no comorbidities, whereas psychological and medical comorbidities were reported in 25% and 17% of the sample, respectively. Regarding the number of depressive episodes, 70 patients had experienced one episode, 17 had experienced two episodes, and four had experienced three episodes. The mean age at onset of depression was 30.26 ± 10.07 years. Regarding treatment, 75 patients received selective serotonin reuptake inhibitors (SSRIs), five received vortioxetine, 12 received polypharmacy, and one received psychotherapy alone. The demographic and clinical characteristics of the participants are presented in Table 1.

**Table 1 Sociodemographic and clinical characteristics of the study participants (N = 92)**

| Characteristic | n (%) |
|---|---|
| **Education** | |
| High school | 14 (15.2) |
| University | 78 (84.8) |
| **Marital status** | |
| Single | 42 (45.7) |
| Married | 45 (48.9) |
| Separated/divorced | 5 (5.4) |
| **Residence** | |
| City | 85 (92.4) |
| Village | 7 (7.6) |
| **Home status** | |
| Owned house | 57 (62.0) |
| Rent house | 35 (38.0) |
| **Occupation** | |
| Employed | 45 (48.9) |
| Unemployed | 47 (51.1) |
| **No comorbidities** | 56 (60.9) |
| **Psychological comorbidity** | |
| Borderline personality disorder | 8 (8.7) |
| Substance use disorder | 3 (3.3) |
| Attention deficit hyperactivity disorder | 2 (2.2) |
| Panic | 1 (1.1) |
| Hair pulling disorder | 1 (1.1) |
| Obsessive-compulsive disorder | 1 (1.1) |
| **Medical comorbidity** | |
| Fibromyalgia | 1 (1.1) |
| Thyroid cancer | 2 (2.2) |
| Breast cancer | 1 (1.1) |
| Neurogenic bladder | 1 (1.1) |
| Diabetes mellitus | 3 (3.3) |
| Hypothyroidism | 3 (3.3) |
| Dyslipidemia | 4 (4.3) |
| Hypertension | 4 (4.3) |
| Thyroidectomy | 1 (1.1) |
| Hysterectomy | 1 (1.1) |
| Polycystic ovarian syndrome | 2 (2.2) |

| | |
|---|---|
| Irritable bowel syndrome | 2 (2.2) |
| **Episodes of depression** | |
| First | 71 (77.2) |
| Second | 17 (18.5) |
| Third | 4 (4.3) |
| **Adversity history** | |
| No adverse life events | 52 (56.5) |
| Adverse life events | 40 (43.5) |
| **Type of treatment** | |
| Selective serotonin reuptake inhibitors | 74 (80.5) |
| Vortioxetine | 5 (5.4) |
| Polypharmacy | 12 (13.0) |
| Psychotherapy only | 1 (1.1) |

Note. Values are presented as n (%). Percentages may not total 100% because of rounding or missing data.

## Changes in Depressive Symptoms and Perceived Cognitive Difficulties

The mean Patient Health Questionnaire-9 (PHQ-9) score decreased from 19.0 ± 5.4 at baseline to 7.1 ± 5.1 after six weeks of treatment (reported $P < 0.0001$). Similarly, the mean Perceived Deficits Questionnaire-5 (PDQ-5) score decreased from 13.0 ± 4.4 at baseline to 7.2 ± 4.0 after six weeks (reported $P < 0.0001$). These findings indicate reductions in depressive symptom severity and self-reported cognitive difficulties over the six-week assessment period.

## Changes in Quality of Life

The WHOQOL-BREF questionnaire showed improvements in general quality of life, general health, and the reported physical, psychological, social-relationships, and environmental domains following treatment. At the facet level, statistically significant changes were reported for most measures. However, no statistically significant differences were reported for financial resources ($P = 0.9$), information and skills ($P = 0.3$), or transport ($P = 0.6$). The comparisons of WHOQOL-BREF scores before and after treatment are presented in Table 2.

**Table 2 Quality-of-life scores before and after treatment**

| Facet/domain | Before treatment | After treatment | P-value |
|---|---|---|---|
| General QOL | 2.5±1 | 3.6±0.8 | <0.0001 |
| General health | 2.3±1 | 3.4±1 | <0.0001 |
| Physical health (Domain 1) | 10±2.6 | 13.9±2.6 | <0.0001 |
| Pain and discomfort | 3±1.4 | 2.2±1 | <0.0001 |
| Energy and fatigue | 2±0.8 | 3±0.8 | <0.0001 |
| Sleep and rest | 2±1 | 3.5±1.1 | <0.0001 |

| | | | |
|---|---|---|---|
| Dependence on medication | 2.7±1.3 | 2.1±1 | 0.0006 |
| Mobility | 3±1.2 | 3.7±0.9 | 0.0001 |
| Activities of daily living | 2±0.9 | 3.5±1 | <0.0001 |
| Working capacity | 2.2±1 | 3.5±1 | <0.0001 |
| Psychological (Domain 2) | 8±2.3 | 12.6±2.3 | <0.0001 |
| Positive feelings | 1.8±0.7 | 2.9±0.7 | <0.0001 |
| Negative feelings | 4±1 | 2.5±1 | <0.0001 |
| Self-esteem | 2±0.9 | 3.5±0.8 | <0.0001 |
| Thinking, learning, memory and concentration | 2±0.9 | 3±0.9 | <0.0001 |
| Body image | 2.5±0.1 | 3.3±0.9 | <0.0001 |
| Spirituality, religion and personal beliefs | 1.9±0.8 | 3±0.8 | <0.0001 |
| Social relationships (Domain 3) | 9±3.2 | 12.8±2.8 | <0.0001 |
| Personal relations | 2.3±1 | 3.3±0.9 | <0.0001 |
| Sex | 2.4±1 | 3±0.9 | <0.0001 |
| Practical social support | 2.5±1.3 | 3.2±1 | <0.0001 |
| Environment (Domain 4) | 12.3±3 | 14.4±7.5 | <0.0001 |
| Financial resources | 3±1 | 3±1 | 0.9 |
| Information and skills | 3.5±1 | 3.6±0.8 | 0.3 |
| Recreation and leisure | 2.3±1.2 | 3±1 | 0.0003 |
| Home environment | 3.3±1.3 | 3.6±1 | <0.0001 |
| Access to health and social care | 3.9±1 | 4±0.9 | <0.0001 |
| Physical safety and security | 2.4±1 | 3.2±0.8 | <0.0001 |
| Physical environment | 2.5±1.2 | 3.1±0.9 | 0.0002 |
| Transport | 3.8±1.2 | 3.9±1 | 0.6 |

Note. Values are presented as mean ± standard deviation (SD). QOL, quality of life.

## One-Year Follow-Up

Longitudinal data was available for 49 participants who completed the one-year follow-up assessment. In this subgroup, the mean PHQ-9 score was 18.1 ± 5.69 at baseline, 8.06 ± 5.79 after six weeks, and 7.0 ± 6.69 at one year. The corresponding mean PDQ-5 scores were 12.7 ± 4.69, 8.06 ± 4.61, and 7.39 ± 4.99, respectively.

Using the study's stated PDQ-5 cutoff score of 12 or higher, cognitive impairment was identified in 28 participants (57.1%) at baseline, 15 participants (30.6%) after six weeks, and eight participants (16.3%) at one year. These findings indicate a reduction in the proportion of participants meeting the study's threshold for perceived cognitive impairment over follow-up. The longitudinal questionnaire scores and the proportion of participants meeting the cognitive-impairment cutoff are presented in Table 3.

**Table 3 Depressive symptoms and perceived cognitive impairment at baseline, 6 weeks, and 1 year (follow-up subgroup, N = 49)**

| Measure | Baseline | 6 weeks | 1 year |
|---|---|---|---|
| PHQ-9 score, mean ± SD | 18.1±5.69 | 8.06±5.79 | 7.0±6.69 |
| PDQ-5 score, mean ± SD | 12.7±4.69 | 8.06±4.61 | 7.39±4.99 |

| | | | |
|---|---|---|---|
| PDQ-5 ≥ 12, n (%) | 28 (57.1%) | 15 (30.6%) | 8 (16.3%) |

Note. PHQ-9, Patient Health Questionnaire-9; PDQ-5, Perceived Deficits Questionnaire-5.

## Associations Between Depressive Symptoms and Perceived Cognitive Difficulties

A positive correlation was observed between PHQ-9 and PDQ-5 total scores at baseline (Spearman's r = 0.67, P < 0.0001) and after six weeks of treatment (r = 0.51, P < 0.0001). These findings indicate that greater depressive symptom severity was associated with greater self-reported cognitive difficulties at both assessment points.

## Associations Between Quality of Life, Depression, and Cognitive Difficulties

The correlation analyses generally demonstrated inverse associations between WHOQOL-BREF scores and both PDQ-5 and PHQ-9 scores at baseline and after six weeks of treatment. These findings suggest that poorer quality of life tends to be associated with greater depressive symptom severity and more pronounced perceived cognitive difficulties. However, not all associations reached statistical significance. For example, the association between general health and PDQ-5 scores after treatment was not statistically significant (r = −0.14, P = 0.2). Similarly, the association between environmental quality of life and PHQ-9 scores after treatment was not statistically significant (r = −0.12, P = 0.2). The correlation coefficients and corresponding P-values are presented in Table 4.

**Table 4 Spearman correlations between quality-of-life domains and cognitive complaints/depressive symptoms**

| QOL domain/facet | PDQ-5: Before (r, P) | PDQ-5: After (r, P) | PHQ-9: Before (r, P) | PHQ-9: After (r, P) |
|---|---|---|---|---|
| General QOL | −0.38, 0.0001 | −0.26, 0.01 | −0.55, <0.0001 | −0.49, <0.0001 |
| General health | −0.24, 0.02 | −0.14, 0.2 | −0.51, <0.0001 | −0.48, <0.0001 |
| Physical health (Domain 1) | −0.37, 0.0003 | −0.50, <0.0001 | −0.57, <0.0001 | −0.76, <0.0001 |
| Psychological (Domain 2) | −0.46, <0.0001 | −0.43, <0.0001 | −0.58, <0.0001 | −0.68, <0.0001 |
| Social relationships (Domain 3) | −0.37, 0.0002 | −0.37, 0.0002 | −0.42, <0.0001 | −0.40, <0.0001 |
| Environment (Domain 4) | −0.52, <0.0001 | −0.21, 0.047 | −0.36, 0.0004 | −0.12, 0.2 |

Note. Values are Spearman correlation coefficients (r) and P-values. QOL, quality of life; PDQ-5, Perceived Deficits Questionnaire-5; PHQ-9, Patient Health Questionnaire-9. Negative coefficients indicate inverse associations.

The changes in mean PDQ-5 and PHQ-9 scores across the three assessment points are illustrated in Figures 1 and 2, respectively.

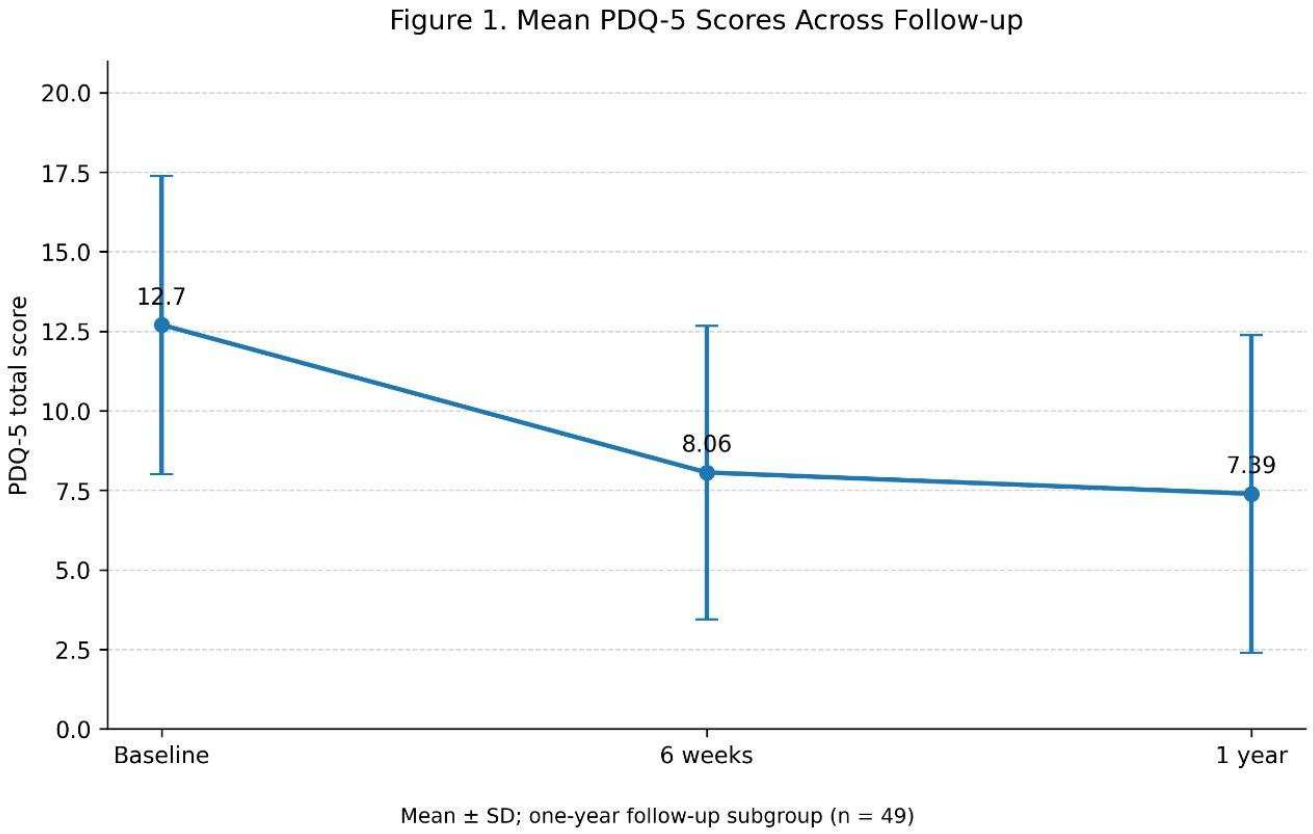



Figure 1. Mean PDQ-5 scores at baseline, six weeks, and one year after treatment among participants who completed the one-year follow-up (n = 49).

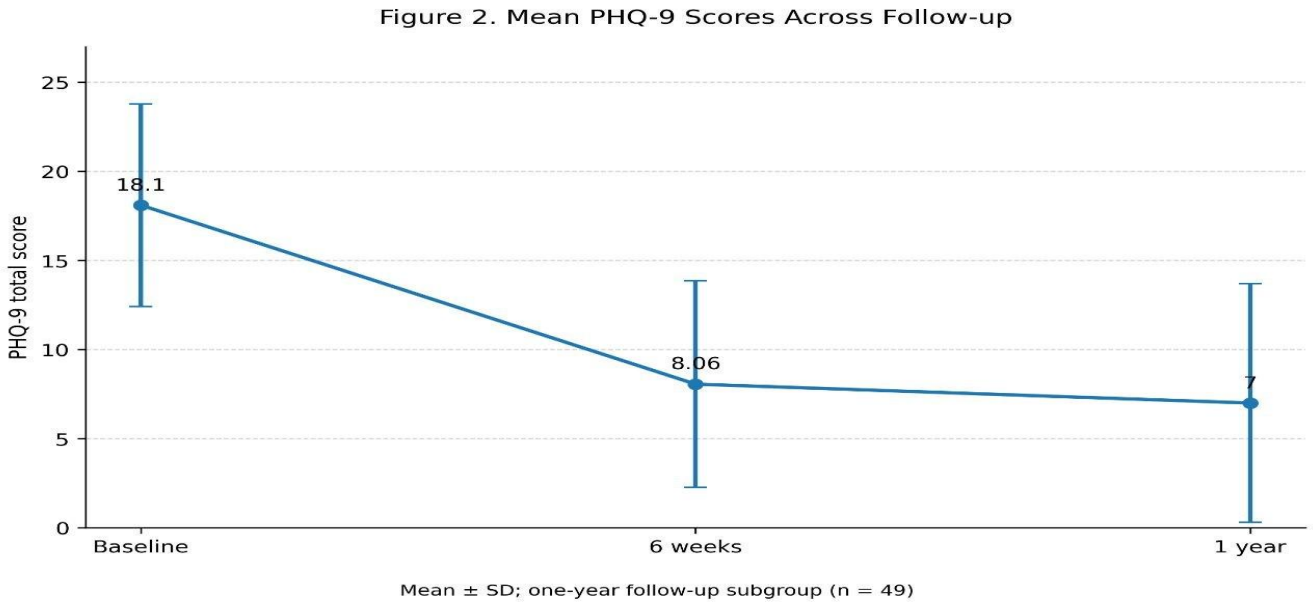



Figure 2. Mean PHQ-9 scores at baseline, six weeks, and one year after treatment among participants who completed the one-year follow-up (n = 49).

## Discussion

In the present study, the proportion of participants meeting the study-defined PDQ-5 threshold decreased from 57.1% at baseline to 16.3% among the 49 participants assessed in one year. These proportions should be interpreted as screen-defined levels of perceived cognitive difficulties rather than confirmed diagnoses of cognitive impairment. Comparisons with previous studies should be made cautiously because the instruments, thresholds, study designs, and assessment time points may differ.

Kriesche et al. conducted a systematic review of the existing literature from 2009 to2019, assessing the extent of cognitive impairment in depression in the acute and remitted states. In the acute phase, they discovered substantial evidence for cognitive impairment, but the impairment was less pronounced in remission (20). These findings approximate the findings of our study, which reported a lower rate of cognitive impairment after one year of treatment compared with the rate of cognitive impairment at baseline. This in part supports the idea that our intervention played an important role in ameliorating

the subjective suffering of people with cognitive impairments. It is not clear whether the antidepressants had a direct effect on cognitive impairments (pro-cognitive effect) or the amelioration of depressive symptoms led to reductions of cognitive impairments that support the state hypothesis of cognitive impairment. The cognitive impairment found after one year may reflect premorbid traits and or toxic effects of depression. Our study shows that greater reduction in cognitive impairment was found at six weeks of treatment which also paralleled the response of depressive symptoms. The findings that subjective cognitive dysfunction is largely secondary to depressive symptoms support the state hypothesis. One of the limitations of this observational study is the use of PDQ-5 that measures the subjective part of cognitive impairment in depression. Lam et al. report indicates that the psychometric validation of the PDQ-5 provides reliability and validity for assessing subjective cognitive dysfunction in patients with MDD (21). They also conclude that neuropsychological tests can assess cognitive performance but are not feasible to be routinely used clinically (21). Sumiyoshi et al. investigated the validity of PDQ-5 and its clinical relevance in Japanese patients with major depressive disorder, and they concluded that PDQ-5 scores adequately represented scores on the PDQ-5(22). It was associated with several measures of functional outcome, depression severity and QOL (12,23). This validates the PDQ- 5 as a reliable tool to assess subjective experience in cognition, which is applicable to time-limited clinical consultations.

Few patients were on vortioxetine in our study and therefore it is difficult to draw any conclusion regarding its pro-cognitive effect. Not only is classical therapeutic management of depression insufficient, but also the administration of first- and second-line anti-depressant shows poor response rates. Current clinical studies have insufficiently investigated for their direct, independent and clinically significant effect on cognition. At present, the only FDA approved antidepressant with pro-cognitive effect on cognitive dysfunction in depression is vortioxetine (24).

### Limitations

This study has several limitations. Its observational design and lack of a control group limit causal conclusions regarding the effects of treatment. The one-year follow-up was available for only 49 participants, which may introduce attrition bias if those followed differed from those not assessed. Cognitive difficulties were evaluated using a self-report questionnaire rather than objective neuropsychological testing. The findings should therefore be interpreted as changes in self-reported symptoms and perceived cognitive difficulties over time.

### Conclusions

We conclude that in daily clinical practice, the administration of PDQ-5 is helpful in estimating the personal experience of cognitive impairment and antidepressant therapy is helpful in ameliorating the subjective complaints, and vortioxetine may affect impairment that does not respond to standard antidepressant therapy.

## Declarations

### Ethics and Human Subjects Issues

This study was approved by the Institutional Review Board at Al-Balqa Applied University (IRB number 526/1/3/26) and conducted in compliance with the ethical statements outlined in the Declaration of Helsinki (17). Written informed consent was obtained from all participants.

### Consent for publication

Not applicable.

## Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Competing interests

The authors declare that they have no competing interests.


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