

Major Depressive Disorder: Psychosocial Impairment and Key Considerations in Functional Improvement

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Abstract

Patients with major depressive disorder (MDD) can experience persistent and substantial functional impairment, and the extent of psychosocial impairment often varies with symptom severity. Factors that may contribute to restoration of psychosocial functioning include the patient's lifetime functional trajectory, the overall effectiveness of depression therapy, and the duration and quality of remission. Patients who achieve full asymptomatic remission from depressive symptoms can still experience functional impairment; thus, restoring psychosocial functioning is increasingly being identified as an important goal of depression therapy. The more effective the therapeutic approach employed to resolve symptoms of depression (eg, long-term duration of treatment, monitoring of patient adherence to treatment, maintenance of asymptomatic remission), the more likely it is that patients with MDD will experience a full restoration of premorbid psychosocial functioning. The goals of this article are to discuss the potential origins of psychosocial impairment, provide literature-based evidence that achieving asymptomatic remission (ie, remission without residual symptoms) is crucial so that functional improvement continues beyond acute-phase treatment, and emphasize the need for an expanded assessment of the illness that fundamentally includes an evaluation of psychosocial functioning, since the restoration of psychosocial functioning does not always accompany the resolution of symptoms in MDD.

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Introduction

Depression is associated with substantial and persistent impairments in psychosocial functioning.¹ Indeed, the criteria for major depressive disorder (MDD) themselves require that qualifying depressive symptoms result in clinically significant distress, as well as impairment in social, occupational, or other areas of functioning. The functional impairment experienced by patients with MDD is often comparable and, in some instances, more profound than that which has been reported among patients suffering from other chronic medical conditions.^{2,4} In addition, although the extent of psychosocial impairment in patients with MDD has been reported to vary according to the duration and severity of the illness, it has also been pointed out that impaired functioning is not always temporally confined to the depressive episode, with subthreshold symptoms often resulting in continued psychosocial impairment despite syndromal remission.^{5,6}

In fact, it has often been described that, when treating most axis I disorders, functional recovery often lags behind symptomatic remission.⁷ For instance, findings of a prospective, longitudinal study of more than 7000 patients who met criteria for at least 1 axis I disorder demonstrated persistent impairment in psychosocial functioning even among patients whose last psychiatric episode occurred more than 12 months prior to the time of assessment. Similarly, in patients with MDD, symptomatic improvement is not always accompanied by restoration of psychosocial functioning, such that patients who achieve a full resolution of depressive symptoms may often still experience functional impairment, although such patients typically report greater functional improvement compared with patients who achieve remission characterized by residual symptoms, or patients who experience little or no symptom improvement.^{1,8,9} Thus, impairment in social functioning may persist for years after the resolution of a major depressive episode, depending on the thoroughness (ie, with vs without residual symptoms) and "stability" (persistence over time) of the remission.

Currently, rapid syndromal and symptomatic remission is the primary goal of treatment for patients with MDD.¹⁰ However, restoring psychosocial functioning to an acceptable, if not premorbid, level is increasingly identified as a significant goal of antidepressant therapy, and a clinical outcome of interest, in addition to improvement in depressive symptoms.^{8,11} Potential factors that contribute to the resto-

ration of psychosocial functioning in MDD include the patient's lifetime functional trajectory, the overall effectiveness of antidepressant treatment, and the duration and quality of remission (Table).

Determinants of Functional Improvement

Lifetime Trajectory

Possible origins of psychosocial impairment include disability that developed during a depressive episode (scar effect), continuation of premorbid disability (trait effect), and disability that results from residual depressive symptoms (state effect).¹² The evaluation of psychosocial dysfunction as a state, trait, or scar effect is a complex undertaking, as it requires a prospective population study including a large patient sample that is evaluated to identify first and recurrent depressive episodes, with assessments of psychosocial functioning before, during, and after the episode.

The population-based Netherlands Mental Health Survey and Incidence Study was the first to evaluate trait, scar, and residual-symptom state effects on functioning in MDD.¹² The results of this study, which defined psychosocial dysfunction as 1 or more deficiencies in the ability to perform specific functions compared with what is considered normal for a specific domain, found modest trait and state effects, but showed that the scar effect does not occur routinely.^{12,13} Specifically, postmorbid psychosocial disability largely reflected the continuation of premorbid psychosocial disability.¹² An estimated 15% to 40% of patients experienced reduced functioning more than 12 months after a major depressive episode compared with the time before the episode occurred.¹³

The finding that the scar effect did not occur frequently is positive, given that treatment nonadherence is often characteristic of patients with chronic illnesses such as MDD.^{14,15} However, the observation that psychosocial functioning is likely impaired long before and after the occurrence of a major depressive episode is significant, and underscores the importance of not only achieving remission of depressive symptoms, but also of normal functioning, in patients with depression.

Antidepressant Treatment

As stated previously, the primary goal of treatment for patients with MDD is the full and sustained resolution of depressive symptoms.¹⁰ In turn, an improvement in psychosocial functioning in MDD has been linked with the absence of residual symptoms of depression as well as the duration of an asymptomatic period following syndromal remission.

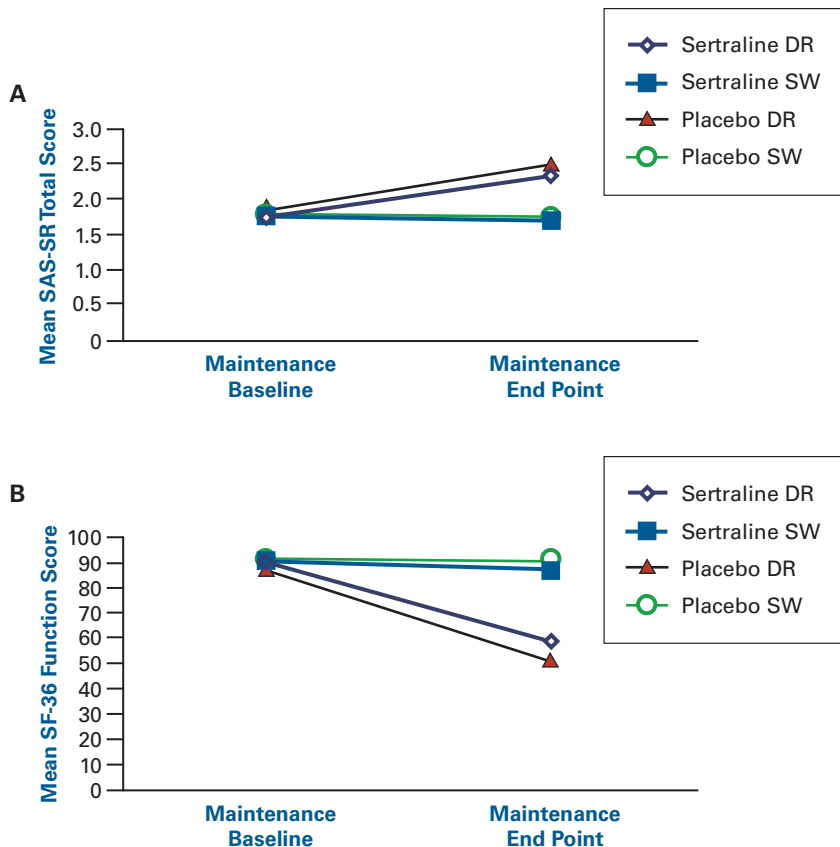
■ **Table. Determinants of Functional Improvement in Patients With Major Depressive Disorder**

Trajectory	Baseline level of functioning predicts posttreatment functioning
Treatment	Necessary for restoration of functioning Resolve symptoms Minimize adverse events
Time	Necessary for restoration of functioning It is crucial to maintain remission because —Functional improvement often lags behind symptomatic improvement in remitters —Loss of remission is associated with a worsening of functioning

Therefore, via its effects on residual symptoms and sustained recovery, depression therapy in itself can also, albeit indirectly, significantly influence the restoration of psychosocial functioning in MDD.⁸ In other words, the more effective the overall therapeutic approach employed to resolve symptoms of depression in patients with MDD (eg, long-term persistency of treatment, monitoring of adherence to medication, maintenance of asymptomatic remission), the more likely the treatment will result in restoration of psychosocial functioning.

Several studies support this relationship. Miller and colleagues,⁹ for example, used 4 assessments of psychosocial functioning, including the Social Adjustment Scale–Self-Report (SAS-SR),¹⁶ the Longitudinal Interval Follow-Up Evaluation (LIFE),¹⁷ the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36),¹⁸ and the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q)¹⁹ in patients with MDD who received 12 weeks of treatment with sertraline or imipramine. Patients treated to full remission (17-item Hamilton Rating Scale for Depression [HAM-D₁₇]²⁰ ≤7) experienced superior psychosocial functioning compared with treatment responders or nonresponders. Specifically, patients who met the criteria for remission demonstrated significantly better overall adjustment (LIFE, SAS-SR), levels of satisfaction (Q-LES-Q, LIFE), marital functioning (SAS-SR), and social functioning (SF-36, LIFE) compared with patients who achieved only a satisfactory therapeutic response or no response ($P \leq .05$ for all comparisons).⁹ Similar results were demonstrated in a separate clinical study by Simon and colleagues,²¹ who reported that patients with MDD who were treated to remission (HAM-D₁₇ ≤7) had significantly fewer missed workdays (6.29 ± 1.06 days) compared with patients who only improved with treatment (HAM-D₁₇, 8-18; 10.37

Figure 1. Relapse of Depressive Symptoms Undermines Improvements in Functional Symptoms Based on SAS-SR (A) and SF-36 (B) Scores in Patients With MDD²²



DR indicates depression re-emergence (defined as *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Revised*, criteria for major depression for ≥ 4 weeks; Clinical Global Impressions [CGI] severity ≥ 4 ; CGI improvement ≥ 3 ; increase in 17-item Hamilton Rating Scale for Depression of ≥ 4 points over maintenance phase baseline, and determination [via patient interview] by a senior investigator of a major depressive episode); MDD, major depressive disorder; SAS-SR, Social Adjustment Scale–Self-Rated; SF-36, Medical Outcomes Study Short Form 36-Item Health Survey; SW, stayed well (defined as absence of DR).

± 1.06 days) or patients with persistent depression (16.80 ± 2.30 days; $P < .001$ for each comparison).²¹

Kocsis et al²² evaluated psychosocial functioning in patients with chronic depression who completed acute (12 weeks) and continuation (16 weeks) treatment with sertraline, sustained a satisfactory response to treatment, and were randomized to maintenance treatment with sertraline or placebo. Based on evaluations using the SAS-SR and SF-36, patients who experienced a depression recurrence during the maintenance phase experienced a significant worsening of psychosocial functioning, losing essentially all functional gains in response to short-term treatment ($P \leq .05$ vs patients who remained well; **Figure 1**).²²

Papakostas and colleagues²³ evaluated psychosocial functioning using the SAS-SR in 222 outpatients with MDD who

received 8 weeks of open-label treatment with fluoxetine. Psychosocial functioning was significantly improved for treatment responders ($\geq 50\%$ reduction in HAM-D₁₇ total score from baseline) versus nonresponders ($P = .0003$), and significantly greater among patients who experienced full remission (HAM-D₁₇ ≤ 7) versus patients who only responded to treatment ($P = .003$). In addition, significant differences in individual SAS-SR scores also were observed among patients who remitted compared with those who only achieved a treatment response, including work outside the home ($P = .046$), extended family ($P = .0007$), and economic functioning ($P = .014$; **Figure 2**).²³

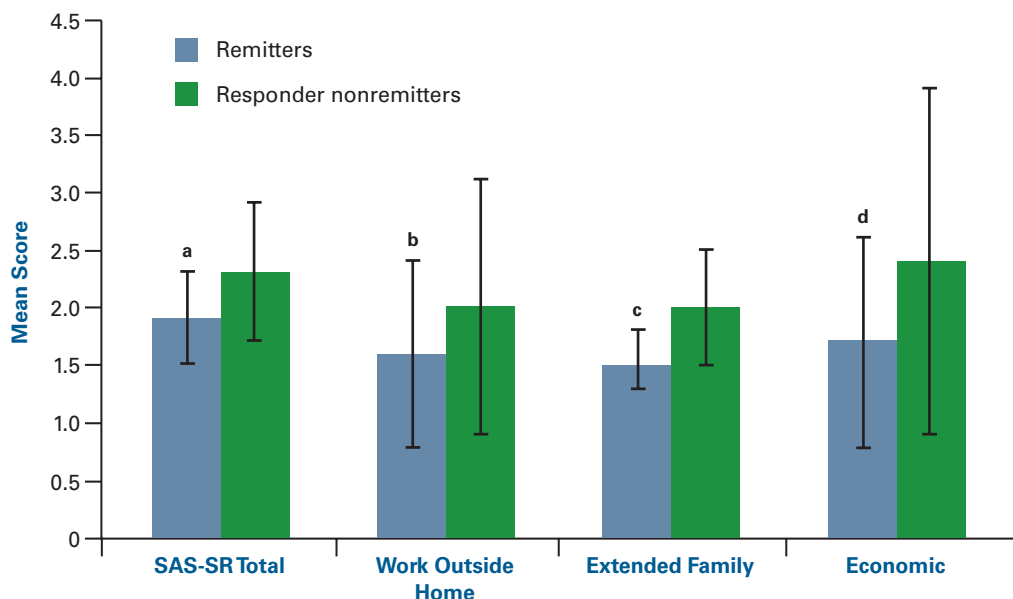
Taken together, these findings add to a growing literature suggesting that patients with persistent depression experience significant impairments in psychosocial functioning compared with nondepressed individuals. In addition, patients who achieve clinical response characterized by syndromal remission with residual symptoms, or achieve response characterized by symptomatic remission, demonstrate progressively greater improvement in psychosocial functioning that is in proportion to the degree of their symptom improvement.²⁴⁻²⁸ Thus, implementing

effective antidepressant therapy is critical to achieve remission of depressive symptoms and impaired functioning, prevent recurrence of depression, and positively impact long-term patient outcomes.

Duration and Quality of Symptom Remission

The duration of symptom remission can also substantially impact long-term functional outcomes for patients with MDD. The clinical study by Papakostas and colleagues²³ previously described was one of the first to demonstrate a relationship between the time of onset of clinical response to antidepressant treatment and degree of improvement in psychosocial functioning based on SAS-SR total scores. Specifically, patients with MDD who experienced an earlier onset of clinical response during the acute phase of treat-

■ Figure 2. Posttreatment Psychosocial Functioning in Patients With MDD Who Achieved Full Remission Versus Patients Who Responded But Did Not Remit²³



MDD indicates major depressive disorder; SAS-SR, Social Adjustment Scale–Self-Report.

^a*P* = .003.

^b*P* < .046.

^c*P* = .0007.

^d*P* = .014.

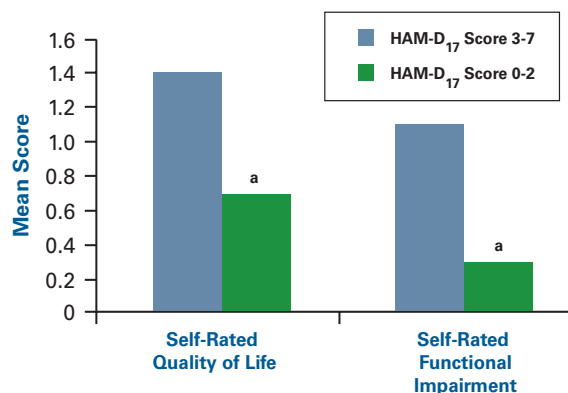
Note: Changes were not significant for housework, family unit, student role, social-leisure activities, parental role, or marital role (*P* > .05 for each).

ment had significantly greater improvements in psychosocial functioning at end point versus patients with late onset of response to treatment (*P* = .04). Furukawa and colleagues²⁹ evaluated patients with MDD who had received no antidepressant treatment within the previous 3 months, and showed that psychosocial functioning, as measured by total scores on the Global Assessment Scale and the SAS-SR, improved with sustained wellness following antidepressant treatment, but did not reach minimal normal ranges until patients achieved recovery (defined as 2 months of symptomatic remission [HAM-D₁₇ < 7]).

The quality and thoroughness of remission is also critical to achieve successful long-term functional outcomes in patients with MDD. In a clinical study of 35 outpatients with MDD, Zimmerman and colleagues³⁰ showed that patients who achieved asymptomatic remission (HAM-D₁₇ < 2) had significantly lower self-rated psychosocial impairment scores (0.3 ± 0.6) compared with patients who experienced partial remission with residual symptoms (HAM-D₁₇ ≤ 7; 0.9 ± 0.7; *P* ≤ .05). In addition, there was a 4-fold difference in the frequency of mild-to-moderate impairment between responders and remitters (40% vs 11.4%, respectively) and between remitters with and without mild residual symptoms (20% vs 5%, respectively), leading the authors to conclude

that the distinction between remission with or without residual symptoms is comparable to that of the distinction between response and remission. In a separate clinical study,

■ Figure 3. Complete Remission Is Associated With Significant Improvements in Self-Rated Functional Impairment and Quality of Life in Patients With MDD³¹



HAM-D₁₇ indicates 17-item Hamilton Rating Scale for Depression; MDD, major depressive disorder.

^a*P* < .01, patients with complete remission (HAM-D₁₇ total score of 0-2) vs patients who achieved broader definition of remission (HAM-D₁₇ total score of 3-7). Quality of life was rated as 0 (very good) to 4 (very bad), and functional impairment rated as 0 (no impairment) to 4 (extreme impairment).

Zimmerman and colleagues³¹ evaluated self-rated quality of life (0 [very good, my life could hardly be better] to 4 [very bad, my life could hardly be worse]) and self-rated functional impairment (0 [no impairment] to 4 [extreme impairment]) in 303 outpatients with MDD, and demonstrated that the presence of residual symptoms during remission negatively impacted quality of life. Compared with patients who met the broader definition of remission (HAM-D₁₇, 3-7), patients who achieved complete remission (HAM-D₁₇, 0-2) had significant improvements in quality of life (1.4 ± 0.7 vs 0.7 ± 0.6 , respectively) and significantly less impaired functioning (1.1 ± 1.0 vs 0.3 ± 0.6) ($P < .01$ for each comparison; **Figure 3**).

The presence of residual symptoms during remission can also adversely impact the long-term functional outcomes of patients by precipitating a relapse of depressive symptoms, thereby having an indirect effect on functioning in MDD. In an early study, Paykel and colleagues³² followed 60 patients for 12 to 15 months after achieving remission of depressive symptoms, and showed that significantly more patients with remission characterized by the presence of residual symptoms (HAM-D₁₇, 8-18) relapsed within a follow-up period of 10 months (76%) compared with patients who achieved remission with no residual symptoms (HAM-D₁₇ <7; 25%; $P < .001$). In a later study, Kennedy and Paykel assessed the original cohort of patients in the above study³² over a follow-up period of 8 to 10 years.³³ Patients with residual symptoms at remission experienced greater long-term impairments in psychosocial functioning compared with patients who achieved remission without residual symptoms. Specifically, on the modified longitudinal SAS at follow-up (mean follow-up, 100 months), more patients who achieved remission with no residual symptoms versus those with residual symptoms had improvements in work functioning (81% vs 42%, respectively; $P = .010$) and marital functioning (81% vs 44%, respectively; $P = .018$). Overall scores on the modified SAS at follow-up were significantly better for remitters with no residual symptoms versus patients with residual symptoms (eg, social functioning [$P = .003$], work functioning [$P = .013$], and extended family relationship [$P = .033$]).³⁵ In addition, remitters with residual symptoms experienced an earlier depression recurrence during the first 2 years of follow-up (42% within 1 year; 56% within 2 years) compared with remitters with no residual symptoms (20% within 1 year; 42% within 2 years). Taken together, these findings suggest that increased residual symptoms, even in patients who have achieved remission, can contribute greater impairment in psychosocial functioning in MDD (directly) and, ultimately, increased risk of depression recurrence (thereby indirectly undermining functional improvement).

Discussion and Conclusions

Restoration of psychosocial functioning is a critical treatment goal for patients who are diagnosed with and receiving antidepressant treatment for MDD. Key factors that impact restoration of functioning include a patient's baseline premorbid level of functioning, the effectiveness of antidepressant therapy in minimizing depressive symptoms and achieving remission, and the duration and quality of remission to further prevent relapse of depression. Continued maintenance treatment with antidepressant therapy after achieving remission is an important approach to improve the duration and quality of remission.

Findings from multiple clinical studies indicate that psychosocial functioning continues to improve over time, but lags behind symptomatic response, such that remission within a short-term clinical trial does not equal recovery, and does not always equal restoration of functioning.²³ Patients who achieve only a clinical response to antidepressant treatment, and not symptomatic remission, as well as patients with remission characterized by the presence of residual symptoms, are at greater risk of relapse of depressive symptoms. Achieving asymptomatic remission without residual symptoms is crucial so that functional improvement continues beyond acute-phase treatment; therefore, the goals of ongoing therapy with antidepressant treatment should include maintenance of remission, prevention of symptom recurrence, restoration of psychosocial functioning, and sustained functional benefits.

In conclusion, standard measures of clinical response and remission that do not adequately capture symptoms of functional impairment are insufficient for achieving successful treatment outcomes in patients with MDD. Future clinical studies evaluating measures of remission to antidepressant treatment should consider a more conceptually valid definition of remission that represents both symptomatic and functional remission. Moreover, the need exists for a functionally expanded assessment of disease severity that fundamentally includes evaluation of psychosocial functioning, as severe impairments in functioning often directly translate to an increased risk of recurrence in patients with MDD.

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