Early Subjective Response to Antidepressants Predicts 12-Week Outcomes Better Than Baseline Severity

Gryan Garcia, Ph.D., Psy.D., FNP-BC, PMHNP-BC (Associate Professor)
Western University of Health Sciences, College of Graduate Nursing, Pomona CA

INTRODUCTION

Major depressive disorder (MDD) is commonly treated with antidepressant therapy in outpatient psychiatric settings, yet treatment response remains variable. In clinical practice, treatment decisions are often influenced by baseline symptom severity, such as initial PHQ-9 scores. However, baseline severity alone may not fully predict who will improve over time. Many patients report early subjective changes, including improved sleep, reduced anxiety, increased energy, better concentration, or improved motivation, before measurable reductions are seen on standardized depression scales.

Prior research suggests that improvement within the first two weeks of antidepressant treatment may be associated with later treatment response and remission. A meta-analysis of 6,562 patients found that early improvement during the first two weeks was predictive of later outcomes in patients with MDD. Other studies have also shown that early symptom-level improvement may help identify patients more likely to respond or remit, although early non-improvement does not always mean treatment failure.

This study examined whether early subjective response within the first two weeks of antidepressant treatment predicted 12-week symptom and functional outcomes more strongly than baseline depression severity.

PURPOSE

The purpose of this study was to evaluate whether early subjective response to antidepressant treatment is a stronger predictor of 12-week clinical outcomes than baseline depression severity among adults with MDD in an outpatient psychiatric setting.

RESEARCH QUESTION

Among adults with MDD initiating a new antidepressant, does early subjective improvement within the first two weeks predict 12-week depressive symptom improvement, remission, and functional improvement better than baseline depression severity?

METHODS

A retrospective cohort study was conducted using outpatient psychiatric records from adults diagnosed with MDD who initiated a new antidepressant between January 2023 and December 2025. Patients were included if they had a documented baseline PHQ-9 score, follow-up documentation within two weeks of medication initiation, and outcome data available at approximately 12 weeks.

Early subjective response was defined as patient-reported improvement in at least one of the following domains within the first two weeks of treatment: sleep, energy, concentration, motivation, or anxiety. Baseline depression severity was measured using the PHQ-9 at treatment initiation. Clinical response was defined as at least a 50% reduction in PHQ-9 score from baseline, consistent with common PHQ-9 response criteria. Remission was defined as a PHQ-9 score below 5, which is commonly used as a remission threshold.

Multivariable regression models were used to examine whether early subjective response predicted 12-week outcomes after adjusting for age, sex, baseline PHQ-9 score, antidepressant class, and comorbid anxiety symptoms.

RESULTS

Overall, 112 patients, or 60.2%, reported early subjective improvement within the first two weeks of antidepressant treatment. The most commonly reported early improvements were sleep, anxiety, energy, motivation, and concentration. Patients with early subjective response had greater improvement in depressive symptoms at 12 weeks compared with patients who did not report early improvement.

Mean PHQ-9 scores decreased from 18.4 to 7.6 among early responders, compared with a decrease from 19.1 to 13.5 among non-early responders. Early responders had a mean PHQ-9 reduction of 10.8 points, while non-early responders had a mean reduction of 5.6 points. Clinical response occurred in 68.8% of early responders compared with 32.4% of non-early responders. Remission occurred in 41.1% of early responders compared with 17.6% of non-early responders.

Table 1. Twelve-Week Outcomes by Early Subjective Response

Outcome	Early Response n = 112	No Early Response n = 74	p-value
Mean PHQ-9 at baseline	18.4	19.1	.31
Mean PHQ-9 at 12 weeks	7.6	13.5	< .001
Mean PHQ-9 reduction	10.8	5.6	< .001
Clinical response	77 (68.8%)	24 (32.4%)	< .001
Remission	46 (41.1%)	13 (17.6%)	.002
Functional improvement	81 (72.3%)	28 (37.8%)	< .001

Functional improvement was also higher among early responders. At 12 weeks, 72.3% of early responders had documented improvement in daily functioning, occupational functioning, school functioning, interpersonal functioning, or self-care, compared with 37.8% of patients without early subjective response.

In adjusted regression analysis, early subjective response remained a significant independent predictor of 12-week clinical response. Patients with early subjective improvement had 3.84 times greater odds of achieving clinical response at 12 weeks compared with those without early improvement, after controlling for demographic and clinical variables. In contrast, baseline PHQ-9 severity was not a consistent independent predictor of remission or functional improvement.

Table 2. Adjusted Predictors of 12-Week Clinical Response

Predictor	Adjusted Odds Ratio	95% Confidence Interval	p-value
Early subjective response	3.84	2.01–7.32	< .001
Baseline PHQ-9 severity	0.96	0.89–1.03	.24
Comorbid anxiety symptoms	0.82	0.44–1.53	.53
SSRI vs. non-SSRI	1.18	0.64–2.19	.59
Age	0.99	0.97–1.02	.61
Female sex	1.11	0.59–2.09	.75

DISCUSSION

The findings suggest that early subjective improvement may be a clinically useful indicator of antidepressant treatment trajectory. Patients who reported improvement in sleep, anxiety, energy, concentration, or motivation within the first two weeks were more likely to experience meaningful symptom reduction, remission, and functional improvement by 12 weeks.

Baseline depression severity was less predictive of outcome. Although baseline PHQ-9 scores are useful for assessing initial symptom burden, they may not fully capture early treatment trajectory or patient-centered improvement. These findings support the importance of asking patients about early changes in functioning and symptom experience, even when standardized scores have not yet significantly improved.

DISCUSSION

This is clinically important because antidepressant treatment often requires timely follow-up, monitoring, and adjustment. CANMAT guidelines emphasize monitoring patients during antidepressant treatment, especially during the early treatment period. Incorporating early subjective response into routine follow-up may help clinicians identify patients who are progressing well and those who may require closer monitoring, dose optimization, augmentation, psychotherapy integration, or medication adjustment.

CONCLUSION

Early subjective improvement within the first two weeks of antidepressant treatment was a stronger predictor of 12-week clinical and functional outcomes than baseline depression severity. Patients who reported early improvements in sleep, anxiety, energy, concentration, or motivation were more likely to achieve symptom response, remission, and functional improvement. These findings support incorporating early subjective response into routine antidepressant monitoring to guide timely, individualized treatment decisions for patients with MDD.

SELECTED REFERENCES

de Vries, Y. A., et al. (2019). Predicting antidepressant response by monitoring early improvement of individual depressive symptoms.

Henkel, V., et al. (2009). Does early improvement triggered by antidepressants predict response/remission?

Kroenke, K., Spitzer, R. L., & Williams, J. B. W. (2001). The PHQ-9: Validity of a brief depression severity measure.

Lam, R. W., et al. (2024). Canadian Network for Mood and Anxiety Treatments clinical guidelines for management of major depressive disorder.

Szegedi, A., et al. (2009). Early improvement in the first two weeks as a predictor of treatment outcome in patients with major depressive disorder: A meta-analysis including 6,562 patients.

RESEARCH POSTER PRESENTATION DESIGN © 2015
www.PosterPresentations.com