

Words: 500 (including Methodological Question Being Addressed and Disclosures)

Title: Establishing the Clinical and Functional Meaningfulness for Changes in the Montgomery-Åsberg Depression Rating Scale

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Methodological Question Being Addressed: Regression models are used to establish relationships between change scores on symptomatic, functional, and quality measures for depression (PHQ-9) and scores on the Clinical Global Impressions–Severity scale. This work can help show the interconnectedness of these scales in terms of a clinically meaningful measure.

Introduction (Aims): The Montgomery-Åsberg Depression Rating Scale (MADRS) is widely used to assess mood symptoms in clinical trials of patients with major depression. Data derived from it are frequently expressed as changes in total scale scores or as changes relative to predefined threshold scores. A limitation of this approach is that there is no well-established definition of a clinically meaningful change for this scale when viewed at the individual-patient level. Clinically meaningful changes in functioning as measured by the Sheehan Disability Scale (SDS) or by the Public Health Questionnaire for depression (PHQ-9) are also unknown. The Clinical Global Impressions–Severity (CGI-S) scale for depression is widely used to measure clinically meaningful symptomatic changes. This analysis explores the relationship between ratings on the MADRS and the CGI-S measured in the same subjects by determining change scores on the MADRS that correspond to a 1- and 2-point change on the CGI-S. Similar relationships for changes are shown for the SDS and the PHQ-9.

Methods: This post hoc analysis used an international clinical trial database (N=223) composed of a 4-week, randomized, placebo-controlled study of antidepressant therapy versus placebo in symptomatic subjects with major depressive disorder who had failed at least 2 prior pharmacologic treatments for their treatment-resistant depression (TRD) within the current episode. All subjects were rated by CGI-S, MADRS, SDS, and PHQ-9. Parametric and nonparametric simple and multiple (with explanatory study design variables for treatment, country, class of antidepressant [SNRI or SSRI], and baseline score) regression models were used to explore relationships between ratings among these scales from baseline to the week-4 endpoint. Clinically meaningful improvement was defined as a 1-point change in the CGI-S scale. A 2-point change on the CGI-S scale was defined as a highly clinically meaningful change. Preliminary data are presented.

Results: A multiple regression model suggested that a 1-point change in the CGI-S scale corresponded to a 6.4-point (SE=0.4) change in the MADRS. Similarly, a multiple regression model suggested that a 1-point change in the CGI-S scale corresponded to a 3.8-point (SE=0.3) change in the SDS. A multiple regression model suggested that a 1-point change in the CGI-S scale corresponded to a 3.1-point (SE=0.2) change in the PHQ-9.

Conclusion: Clinically meaningful improvement at a patient level in depressive symptoms identified by the CGI-S scale corresponds to approximately 6.4-, 3.8-, and 3.1-point improvement from baseline on the MADRS, SDS, and PHQ-9 scales, respectively, in subjects with TRD. Additional studies are needed

to confirm these findings in subjects who demonstrate broader ranges of change and to show that these relationships hold for both clinical worsening and improvement.

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