# What Is the Threshold for Symptomatic Response and Remission for Major Depressive Disorder, Panic Disorder, Social Anxiety Disorder, and Generalized Anxiety Disorder?

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**Objective:** Symptom-free remission is a goal for treatment in depression and anxiety disorders, but there is no consensus regarding the threshold for determining remission in individual disorders. We sought to determine these thresholds by comparing, in a post hoc analysis, scores on the Clinical Global Impressions scale (CGI) and disorder-specific symptom severity rating scales from all available studies of the treatment of major depressive disorder, panic disorder, generalized anxiety disorder, and social anxiety disorder with the same medication (escitalopram). We also sought to compare the standardized effect sizes of escitalopram for these 4 psychiatric disorders.

Data Sources and Study Selection: Raw data from all randomized, double-blind, placebocontrolled, acute treatment studies sponsored by H. Lundbeck A/S (Copenhagen, Denmark) or Forest Laboratories, Inc. (New York, N.Y.), published through March 1, 2004, with patients treated with escitalopram for DSM-IV major depressive disorder (5 studies), panic disorder (1 study), generalized anxiety disorder (4 studies), or social anxiety disorder (2 studies) were compared with regard to the standardized effect sizes of change in CGI score and scores on rating scales that represent the "gold standard" for assessment of these disorders (the Montgomery-Asberg Depression Rating Scale, the Panic and Agoraphobia Scale, the Hamilton Rating Scale for Anxiety, and the Liebowitz Social Anxiety Scale, respectively).

**Data Synthesis:** In all indications, treatment with escitalopram showed differences from placebo in treatment effect from 0.32 to 0.59 on the CGI-S and CGI-I and standardized effect sizes from 0.32 to 0.50 on the standard rating scales. There were no significant differences among the different disorders. Moderate to high correlations were found between scores on the CGI and the standard scales. The corresponding standard scale scores for CGI-defined "response" and "remission" were determined.

*Conclusion:* Comparison of scores on the standard scales and scores on the CGI suggest that the traditional definition of response (i.e., a 50% reduction in a standard scale) may be too conservative.

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n clinical studies, treatment outcome is commonly assessed by using both a global measure and a disorderspecific scale. The Clinical Global Impressions scales (CGI)<sup>1</sup> are commonly used as global measures for disease severity and treatment-induced improvement in a variety of disorders both in psychiatry and in other areas. The CGI scales require the clinician to rate the overall severity of the patient's illness at the time of assessment, relative to the clinician's past experience with patients who have the same diagnosis, by considering all aspects of the disorder (CGI-Severity of Illness, or CGI-S) and to rate the patient's overall improvement compared with baseline (CGI-Improvement, or CGI-I). The CGI has high "face validity"; i.e., scale scores are defined by common sense, corresponding to the language that clinicians use when talking about efficacy of a certain treatment. "Response" very clearly corresponds to "much" or "very much improved" on the CGI-I, while "remission" matches up to "not at all ill" or "borderline mentally ill" on the CGI-S.

Treatment outcome is also measured by using disorderspecific scales that include a number of items, each of which covers separate aspects of the disorder. For depression and anxiety disorders, standard scales exist that are applied routinely in most clinical trials. These disorder-specific scales include the Montgomery-Asberg Depression Rating Scale (MADRS)<sup>2</sup> for major depressive disorder (MDD), the Hamilton Rating Scale for Anxiety (HAM-A)<sup>3</sup> for generalized anxiety disorder (GAD), and the Liebowitz Social Anxiety Scale (LSAS)<sup>4</sup> for social anxiety disorder (SAD). For panic disorder, disorder-specific scales have been developed only recently. The Panic and Agoraphobia Scale (PAS)<sup>5</sup> and a similar scale, the Panic Disorder Severity Scale (PDSS),<sup>6</sup> have been used increasingly in randomized controlled clinical trials in panic disorder and have been recommended by the European Medicines Agency (EMEA) for use in panic disorder studies.<sup>7</sup>

There has been some controversy about what can be defined as a clinically meaningful change in symptoms on a rating scale. Possible definitions include (1) a difference of  $\geq$  1.96 standard deviations from the mean of the ill population, (2) a difference of  $\leq 1.96$  standard deviations from the healthy population (which requires the existence of a normative data for the scale), and (3) a scale score nearer to the mean of the healthy population than the mean of the ill population. Also, a "reliable change index" has been proposed as cutoff score for meaningful improvement, which is based on the means and standard deviations of the scale scores and the test-retest reliability of a scale.<sup>8</sup> Nevertheless, these definitions are not typically used in everyday practice. Instead, "response" is commonly defined as  $a \ge 50\%$  reduction on the commonly used standard scales. However, this definition is arbitrary, and cutoff points might be better based on a clinically measurable improvement.

The definition of "remission" on standard scale scores is sometimes based on a cutoff score (e.g.,  $\leq 7$  on the HAM-A) and varies from study to study. It has been discussed that the definition of remission should not be based only on a single scale consisting of a number of anxiety symptoms, such as the HAM-A, but should also include measures of quality of life. Therefore, work groups have suggested comprehensive definitions of remission. Ballenger et al.<sup>9</sup> have suggested a complex algorithm for defining remission in anxiety disorders, consisting of cutoff scores on measures specific for a certain anxiety disorder (e.g., the HAM-A or the LSAS), a depression scale (HAM-D), quality-of-life measures (the Sheehan Disability Scale), and a panic frequency measure in the case of panic disorder. While these extensive definitions have the advantage of giving a complete picture of the patient's improvement, the psychometric properties of these algorithms have not been tested.

It has been suggested that a cutoff score should be determined on a scale that has tested psychometric properties and that covers all aspects associated with an impairment of quality of life.<sup>10</sup> In contrast to some rating scales like the HAM-A, which consist only of a list of anxiety symptoms, the PDSS<sup>6</sup> and the PAS<sup>5</sup> are comprehensive scales that cover all domains that are dysfunctional in panic disorder: panic attacks, agoraphobic avoidance, anticipatory anxiety, impairment in work and social situations, and fear of physical sensations. Thus, for panic disorder, the definition of remission could be based on a cutoff score on 1 of these 2 scales, preferably together with a measure of depression.<sup>11</sup>

A definition of remission should also address the question of time course. Criteria for remission should not only be fulfilled at one timepoint, but should remain stable for a certain period of time (e.g., 8 consecutive weeks).

Selective serotonin reuptake inhibitors (SSRIs) represent the mainstay of pharmacologic treatment in patients with major depression or anxiety disorders.<sup>12,13</sup> Escitalopram, an SSRI, has been shown to be effective in a number of randomized placebo- and comparator-controlled trials in MDD and 3 major anxiety disorders (panic disorder, GAD, and SAD). It is also effective in treating anxiety symptoms in patients with depression.<sup>14</sup>

Analysis of studies of the treatment of depression and 3 different anxiety disorders with the same medication provides an opportunity to determine the threshold for "response" and "remission" by comparing scores on the CGI and standard rating scales; we have conducted such an analysis for all published placebo-controlled studies with escitalopram.

To our knowledge, this is the first comprehensive investigation of the comparative efficacy of one drug across different mood and anxiety disorders. By comparing the standardized effect sizes of the same treatment on scores on the CGI and standard rating scales, we can determine whether the same treatment yields different standardized effect sizes in different disorders.

#### **METHOD**

The study included raw data from all randomized, double-blind, placebo-controlled, acute treatment studies sponsored by H. Lundbeck A/S (Copenhagen, Denmark) or Forest Laboratories, Inc. (New York, N.Y.) completed as of March 1, 2004, in which patients were treated with escitalopram for DSM-IV MDD (5 studies, N = 1992), panic disorder (1 study, N = 351), GAD (4 studies, N = 1514), or SAD (2 studies, N = 1178) and in which the CGI had also been used (Table 1). Some of these studies also included a comparator drug. Further details of these studies are available in the primary publications.

In all studies, patients were assessed on the CGI-S and CGI-I. The CGI-I requires the clinician to rate how much the patient's illness has improved or worsened relative to a baseline state (1 = very much improved, 2 = much improved, 3 = minimally improved, 4 = no change, 5 = minimally worse, 6 = much worse, 7 = very much

Table 1. Schematic Presentation of Double-Blind, Placebo-Controlled, Acute Treatment Studies of Escitalopram, by Diagnosis, Included in the Analysis

Study	Duration, wk	Doses (mg/d) and ITT N
MDD		
$1^{15}$	8	PBO (N = 189)
		ESC 10 (N = 188)
$2^{16}$	8	PBO (N = 154)
		ESC 10–20 (N = 155)
		CIT 20–40 (N = 159)
$3^{17}$	8	PBO (N = 119)
		ESC 10 (N = 118) and 20 (N = 123)
		CIT 40 (N = 125)
$4^{18}$	8	PBO (N = 125)
		ESC 10–20 (N = 124)
		CIT 20–40 (N = 119)
$5^{19}$	8	PBO (N = 151)
		ESC 10–20 (N = 143)
SAD		
$6^{20}$	12	PBO (N = 176)
21		ESC 10–20 (N = 177)
$7^{21}$	24	PBO (N = $165$ )
		ESC 5 (N = 166), 10 (N = 164),
		20 (N = 163)
		PAR 20 (N = 167)
GAD		
822	12	PBO (N = $138$ )
		ESC 5 (N = 134), 10 (N = 134),
		20 (N = 132)
~ 23		PAR 20 (N = 136)
925	8	PBO(N = 128)
1023	0	ESC $10-20$ (N = 124)
1025	8	PBO(N = 138)
1 . 24	0	ESC $10-20$ (N = 143)
1124	8	PBO(N = 153)
DD		ESC $10-20$ (N = 154)
PD 10 <sup>25</sup>	10	$\mathbf{D}\mathbf{D}\mathbf{O}$ (N = 114)
1220	10	PBO(N = 114)
		ESU 5-20 (N = 125)
		C11 10-40 (N = 112)

Abbreviations: CIT = citalopram, ESC = escitalopram, GAD = generalized anxiety disorder, MDD = major depressive disorder, PAR = paroxetine, PBO = placebo, PD = panic disorder, SAD = social anxiety disorder.

worse). For the CGI-S, the investigator indicates the overall severity of the patient's illness, considering all aspects of the disorder and comparing the patient with other patients with the same disorder on a simple 1-through-7 Likert scale (1 = normal [not at all ill], 2 = borderline mentally ill, 3 = mildly ill, 4 = moderately ill, 5 = markedly ill, 6 = severely ill, 7 = extremely ill). "Response" on the CGI is conventionally defined as a CGI-I score of  $\leq 2$  ("very much improved or much improved") and "remission" as a CGI-S score of  $\leq 2$  ("normal/not at all ill or borderline mentally ill").

For each of these 4 disorders, one disorder-specific symptom severity rating scale was also used, including the MADRS for studies in MDD, the PAS for panic disorder, the HAM-A for GAD, and the LSAS for SAD.

### **Statistics**

All analyses were based on the full analysis set (FAS), which corresponds to a modified intent-to-treat (ITT)

analysis (i.e., intake of at least 1 dose of study drug and 1 postbaseline efficacy assessment were required). Analyses of covariance (ANCOVAs) were performed, adjusting for baseline value, center, and treatment. In case of dropouts, the last-observation-carried-forward (LOCF) method was used for all ANCOVAs. Within each indication, CGI-S scores were equated to the disorder-specific symptom severity rating scale by finding, for each value on the CGI-S, the corresponding value on each scale. For example, if 42% of patients scored  $\leq 2$  on the CGI-S, and 42% scored  $\leq$  11 on the MADRS, then a CGI-S score  $\leq$  2 corresponds to a MADRS score  $\leq$  11. Similarly, CGI-I score was equated to the percent decrease from baseline in each disorder-specific symptom severity rating scale. This was done by looking at all observations (observed cases analysis) after baseline for patients from all treatment groups (N = 5035). As the study duration varied across the trials, the equating at each timepoint was tested in order to check whether the cutoffs were depending on time. However, the variation over time was low, which allowed us to make a combined analysis over all timepoints.

Standardized effect sizes of the differences were calculated by using Cohen's d.<sup>26</sup> Different methods were used to derive d from the data presented within the different studies. Since our main goal was to calculate standardized effect sizes for direct comparisons between different types of treatment within each study, d represents differences between preoutcome and postoutcome of 2 treatments compared, divided by a pooled standard deviation, using the following formula:

$$d = \frac{(treat1_{pre} - treat1_{post}) - (treat2_{pre} - treat2_{post})}{SD_{average}}$$

Effect sizes can be interpreted as small ( $\ge 0.20$ ), medium ( $\ge 0.50$ ), or large ( $\ge 0.80$ ).

Spearman rank correlation coefficients were used for correlations between scores on the CGI-S/CGI-I and the standard scales. All pairs of assessments at all timepoints were included in the calculations of these correlations, with the exception of the baseline assessment, for which no CGI-I scores are available.

In this analysis, remission criteria on the disorderspecific scales are determined by equating scores on these scales to the CGI-S score. Another possibility would have been to use receiver operating characteristic (ROC) methods, which aim to minimize the false positive and the false negative rate. This is a good method when the true positives and the true negatives can be considered fairly constant with time. That is, however, not the case for remission in mood disorder trials, in which the percentage of true positives (i.e., the CGI-S remitters) will increase over time and will vary significantly across studies. With different true positive rates, the ROC method will give different cutoff values for remission on the disorderspecific scale. In particular, true positives do not occur at Figure 1. Mean Difference in Treatment Effect as Measured by the CGI-S at Endpoint Between Escitalopram- and Placebo-Treated Patients, by Disorder<sup>a</sup>



<sup>a</sup>The standardized effect sizes may be calculated by dividing these differences by the corresponding standard deviations, which are 1.16 (PD), 1.04 (GAD), 1.10 (SAD), and 1.16 (MDD). Abbreviations: CGI-S = Clinical Global Impressions-Severity of

baseline, so neither can false negatives. The ROC method will, therefore, minimize only the false positives, which is best done by setting the remission criterion on the disorder-specific scale to 0, thereby insuring that there are no positives. Since remission should be evaluated after treatment, rather than at baseline or during the trial, the ROC method should be used only at the timepoint where remission is desired, usually the trial endpoint.

#### RESULTS

Treatment with escitalopram was associated with significant placebo–active drug differences across all indications (p < .001) on both the CGI-S (Figure 1) and CGI-I (Figure 2), shown by treatment effects ranging from 0.32 to 0.59. A numerically larger treatment effect was found in panic disorder than in the other indications, but this difference was not statistically significant.

Also, the standard scales showed significant differences between escitalopram and placebo (p < .001), with standardized effect sizes ranging from 0.32 to 0.50. The highest standardized effect size was found in panic disorder when compared with other disorders (Figure 3).

There were high correlation coefficients between scores on the CGI scales and scores on the standard scales for all disorders with the exception of panic disorder, for which only moderate correlations were found (Table 2 and Figure 4). All correlations were statistically significant (p < .001).

CGI-I-defined response corresponded to 39%, 23%, 42%, and 31% reductions in scores on the MADRS, PAS, HAM-A and LSAS, respectively (Table 3). CGI-S-defined remission corresponded to a score of 11 on the

Figure 2. Mean Difference in Treatment Effect as Measured by the CGI-I at Endpoint Between Escitalopram- and Placebo-Treated Patients, by Disorder<sup>a</sup>



<sup>a</sup>The standardized effect sizes may be calculated by dividing these differences by the corresponding standard deviations, which are 1.07 (PD), 1.00 (GAD), 1.02 (SAD), and 1.12 (MDD).

Abbreviations: CGI-I = Clinical Global Impressions-Improvement scale, GAD = generalized anxiety disorder, MDD = major depressive disorder, PD = panic disorder, SAD = social anxiety disorder.

MADRS, a score of 11 on the PAS, a score of 9 on the HAM-A, and a score of 36 on the LSAS (Table 4).

#### DISCUSSION

Improvement rates, as measured by Cohen's d, achieved by escitalopram treatment were not different between depression and the anxiety disorders. While standardized effect sizes were numerically higher for panic disorder, this difference from other diagnoses was not statistically significant. Effect size differences from placebo correlated satisfactorily between scores on the standard scales and the CGI ratings.

The CGI was shown to be a reliable measure of disease severity and to be sensitive to change. Treatment effects for placebo–active drug differences did not differ between the CGI ratings and scores on the standard scales. High correlations were found between CGI and standard ratings for all disorders with the exception of panic disorder, for which only moderate correlations were found. This may be due to the fact that this correlation was based on only 1 study, in which the CGI was not the primary efficacy variable. In another comparison of CGI and the PAS scores, a much higher correlation of 0.91 was found.<sup>27</sup>

As the CGI is easily interpretable, simple, and not time-consuming, the question might arise: If the CGI shows the same treatment effects as standard scales, do we still need symptom-specific scales? We believe there is such a need, for the following reasons. First, the CGI is a relative measure, depending on the clinician's past experience with patients who have the same diagnosis, whereas symptom-specific scales are more absolute measures, potentially making the results more comparable

Illness scale, GAD = generalized anxiety disorder, MDD = major depressive disorder, PD = panic disorder, SAD = social anxiety disorder.

Figure 3. Standardized Effect Sizes (Cohen's d) of Total Scores on Disorder-Specific Rating Scales Between Escitalopram- and Placebo-Treated Patients



Abbreviations: GAD = generalized anxiety disorder, HAM-A = Hamilton Rating Scale for Anxiety, LSAS = Liebowitz Social Anxiety Scale, MADRS = Montgomery-Asberg Depression Rating Scale, MDD = major depressive disorder, PAS = Panic and Agoraphobia Scale, PD = panic disorder, SAD = social anxiety disorder.

among different patient samples. Second, the reliability (Cronbach  $\alpha$ ) of a scale rises with higher number of scale items, whereas the reliability of the CGI, which has only 1 item, is rather low. Third, the CGI does not allow differentiated assessments, whereas disorder-specific standard scales may be evaluated item by item or by using subscales. For example, the PAS includes subscales such as "agoraphobic avoidance" and "anticipatory anxiety," which allow for specific assessment of certain aspects of a disorder.

When defining "response" to a treatment on a standard rating scale,  $a \ge 50\%$  reduction of scale score is conventionally used as the cutoff point. Nevertheless, this is an arbitrary decision, particularly in view of the fact that scales that measure depression and anxiety are not necessarily entirely linear (unlike, say, measurement of height or weight). Indeed, in this analysis the CGI-I definition of at least "much improved" corresponded to only 39%, 23%, 42%, and 31% reductions in the MADRS, PAS, HAM-A, and LSAS, respectively, suggesting that the usual 50% definition may be too conservative, with a clinically measurable difference at a smaller change from baseline. A controlled clinical trial has the greatest power to differentiate between the effects of medication and placebo when the chosen cutoff splits the group equally into responders and nonresponders.

On the other hand, a score of "much improved" on the CGI-I may not represent a clinically meaningful enough change in symptoms, as patients with this score may still show substantial symptomatology. There should be a shift toward more comprehensive definitions of response and remission compared to placebo as our choices of safe and effective treatment options have grown and the risk of

Table 2. Spearman Rank Correlation Coefficients Between
CGI-S/CGI-I Score and Mean Total Scores on Standard
Rating Scales <sup>a</sup>

	Correlation (r)		
Rating Scale	CGI-S	CGI-I	
MADRS	0.82	0.86	
PAS	0.67	0.51	
HAM-A	0.83	0.86	
LSAS	0.81	0.85	

<sup>a</sup>CGI-I score was correlated to percent reduction from baseline rather than absolute reduction from baseline. All correlations were significant (p < .001).

Abbreviations: CGI-I = Clinical Global Impressions-Improvement scale, CGI-S = Clinical Global Impressions-Severity of Illness scale, HAM-A = Hamilton Rating Scale for Anxiety, LSAS = Liebowitz Social Anxiety Scale, MADRS = Montgomery-Asberg Depression Rating Scale, PAS = Panic and Agoraphobia Scale.

residual symptoms resulting in future relapse in anxiety disorders and depression disorders has become more clear.

"Remission" is usually defined as a CGI-S score of  $\leq 2$ ("not at all ill" or "borderline mentally ill"). This can be further divided into "complete" or "symptom-free" remission that can be defined as a CGI-S score of 1 ("not at all ill"), and remission defined as a CGI-S score of 2 or less ("borderline mentally ill").

For disorder-specific scales, a cutoff point is conventionally defined prospectively in clinical studies. These cutoff points are arbitrary and may differ from study to study. For example, MADRS scores of  $\leq 9$ ,<sup>28</sup>  $\leq 10$ ,<sup>29</sup>  $\leq 11$ ,<sup>30,31</sup> and  $\leq 12^{32}$  have been used to define remission. One analysis of 684 patients yielded optimal definitions of remission of scores of  $\leq 10$  or  $\leq 11$  on the MADRS.<sup>33</sup> These authors included baseline data in their calculations, which is why an artificially low criterion for remission was found for the MADRS. In their data (see Figures 1 and 2 from Hawley et al.<sup>33</sup>), 29.6% of patients had a CGI-S score  $\leq 2$  while only 19.3% of patients had a MADRS score < 9 and 22.0% had a MADRS score < 10. These MADRS remission criteria are, therefore, more strict than CGI-S score  $\leq 2$ . In fact, 29.4% of their patients had a MADRS score  $\leq 12$ .

Hawley et al.<sup>33</sup> did not use CGI-S score  $\leq 2$  as the criterion for remission; instead, they categorized all patients with a CGI-S score of 1 and one half of the patients with a score of 2 as having achieved remission since such a grouping of patients represents the cusp between a mildly symptomatic and an asymptomatic state. This covers 21.7% of their ratings, and with this interpretation of CGI-S score = 2, a MADRS score < 10 gives a similar percentage of remitters. We believe that it is better to consider a CGI-S score of 2 or less as indicating remission and a CGI-S score of 1 as indicating complete or symptom-free remission. Our analysis thus suggests that a MADRS score of 11 or less represents remission from depression. A CGI-S score of 1 corresponds to a



Figure 4. Correlation Between Postbaseline Scores on the CGI-S and the (a) MADRS, (b) HAM-A, (c) LSAS, and (d) PAS<sup>a,b</sup>

<sup>a</sup>Correlation coefficients are Spearman rank correlation coefficients. <sup>b</sup>Remission corresponds to a CGI-S score of 2, and complete or symptom-free remission corresponds to a CGI-S score of 1. Abbreviations: CGI-S = Clinical Global Impressions-Severity of Illness scale, HAM-A = Hamilton Rating Scale for Anxiety, LSAS = Liebowitz Social Anxiety Scale, MADRS = Montgomery-Asberg Depression Rating Scale, PAS = Panic and Agoraphobia Scale.

Table 3. Corresponding CGI-I Values for Mean Percent	
Changes From Baseline in Total Scores on Standard	
Rating Scales	

	Mean Percent Change From Baseline			
CCL I Sama	MADRS	PAS	HAM-A	LSAS
CGI-I Score"	(MDD)	(PD)	(GAD)	(SAD)
1 (very much improved)	70	51	72	63
2 (much improved)	39	23	42	31
3 (minimally improved)	13	-3	15	10
4 (no change)	-10	-34	-9	-9

<sup>a</sup>For CGI-I score > 4, there were too few patients determining the corresponding standard scale percentages (response is traditionally defined as CGI-I score ≤ 2).

Abbreviations: CGI-I = Clinical Global Impressions-Improvement scale, GAD = generalized anxiety disorder, HAM-A = Hamilton Rating Scale for Anxiety, LSAS = Liebowitz Social Anxiety Scale, MADRS = Montgomery-Asberg Depression Rating Scale, MDD = major depressive disorder, PAS = Panic and Agoraphobia Scale, PD = panic disorder, SAD = social anxiety disorder.

MADRS score of  $\leq 5$  and may be regarded as "complete" or "symptom-free" remission. This might be a more appropriate remission criterion in long-term trials and is close to the strict definition of MADRS score  $\leq 4$  suggested by Zimmerman et al.,<sup>34</sup> which is based on MADRS values for healthy control subjects. For the PAS, a cutoff score of  $\leq 11$  is suggested by the present analysis, but this

## Table 4. Corresponding CGI-S Values for Mean Total Scores on Standard Rating Scales

	Mean Total Score			
CGI-S Score <sup>a</sup>	MADRS (MDD)	PAS (PD)	HAM-A (GAD)	LSAS (SAD)
1 (not at all ill)	5	8	4	19
2 (borderline ill)	11	11	9	36
3 (mildly ill)	19	18	15	59
4 (moderately ill)	29	29	24	86

<sup>a</sup>For CGI-S score > 4, there were too few patients to be able to equate the CGI-S scores with the standard scale scores (remission is traditionally defined as CGI-S score  $\leq 2$ ).

Abbreviations: CGI-S = Clinical Global Impressions-Severity of Illness scale, GAD = generalized anxiety disorder, HAM-A = Hamilton Rating Scale for Anxiety, LSAS = Liebowitz Social Anxiety Scale, MADRS = Montgomery-Asberg Depression Rating Scale, MDD = major depressive disorder, PAS = Panic and Agoraphobia Scale, PD = panic disorder, SAD = social anxiety disorder.

is based on only 1 study. For the HAM-A, cutoffs between  $\leq 7$  and  $\leq 10$  have been used for the definition of remission.<sup>9,35–37</sup> Some authors have suggested even lower scores as cutoff margin.<sup>34</sup> Our findings suggest a cutoff score of  $\leq 9$ . For social anxiety disorder, an LSAS score of  $\leq 30$  has been suggested to define remission<sup>9,37</sup>; our findings suggest an LSAS cutoff score of 36.

The present analysis has limitations, as the trials analyzed do not include patients with comorbid disorders. Moreover, this was a post hoc analysis of trials that were planned for assessing the efficacy of escitalopram. Study duration varied across the trials; although we did not find a substantial influence of time, this is a limitation, as a number of studies on anxiety disorders have demonstrated continued response up to 6 months.<sup>38–42</sup>

Nevertheless, the current database allows a consideration of the psychometrics of the CGI across a range of mood and anxiety disorders. The analysis demonstrates that the CGI is a robust measure across the mood and anxiety disorders. Furthermore, the analysis provides a systematic approach toward determining response and remission cutoffs on the standard symptom rating scales used in these disorders.

Drug name: escitalopram (Lexapro).

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