

Treatment of Anxiety Disorders to Remission

James C. Ballenger, M.D.

Treating anxiety disorders to remission should be the goal of all practitioners. A remitted patient should be well, both in symptoms and function, and be indistinguishable from a never-ill counterpart. The definition of remission in patients with anxiety disorders should also be clear, practical, and easy to use. It is useful to measure response in an objective way, such as with standardized instruments appropriate for the disorder, and to develop remission criteria specific to each disorder. This article proposes remission criteria, using standardized measures, for 5 common anxiety disorders: panic disorder, social anxiety disorder, generalized anxiety disorder, obsessive-compulsive disorder, and post-traumatic stress disorder.

(J Clin Psychiatry 2001;62[suppl 12]:5-9)

According to Frank et al.,¹ remission in depression is a time period in which the severity of symptoms has decreased so that the patient no longer meets diagnostic criteria for the disorder, although some minimal symptoms may persist. The importance of remission is clear in the treatment of depression: patients with major depressive disorder usually fail to regain full functional recovery until they are treated to resolution of their symptomatology.² Moreover, depressed patients have fewer relapses and recurrences if the index episode is treated to remission.³ The evidence is less clear for the anxiety disorders, but it makes sense that treating to remission would have the same importance in these disorders. This article will discuss the treatment to remission of panic disorder, social anxiety disorder, generalized anxiety disorder (GAD), obsessive-compulsive disorder (OCD), and posttraumatic stress disorder (PTSD) and encourage the use of objective measures in defining remission.

DEFINITION OF REMISSION IN ANXIETY DISORDERS

In anxiety disorders, the clinician has many reasons to ensure that patients achieve remission. These disorders are generally chronic and recurring,⁴⁻⁸ and such chronic illnesses have a heavy economic toll. According to Greenberg et al.,⁹ in 1990, the direct and indirect costs of

anxiety disorders in the United States was \$42.3 billion. The average person with an anxiety disorder is sick for many years before seeking treatment; in GAD, for example, the length of time between onset and first treatment averages 15 years.¹⁰ After being ill for so many years, some patients may want to stop treatment at the first sign of improvement, because they are either pleased with the result or fearful of taking medication (for example, "becoming dependent on the medicine"). Discontinuing treatment too soon can result in patients who are only partially improved and still partially ill, an outcome that the clinician must guard against. Unfortunately, patients who experience some improvement from treatment will at times settle for that instead of continuing treatment to remission.

The specific definition of remission in patients with anxiety disorders should be clear as well as practical. Frank and colleagues'¹ definition of remission in depression implies that a patient is either mildly symptomatic or free of symptoms. A more stringent definition of remission would be that the treated patient is essentially indistinguishable from healthy or never-ill counterparts. This level of recovery is a step beyond no longer meeting diagnostic criteria; the patient must have no symptoms, subclinical or otherwise, that suggest the particular anxiety disorder for which he or she was treated ever occurred.

An additional aspect of remission is that of time to recovery, both symptomatic and functional. Symptomatic recovery generally precedes functional recovery, and a remitted patient is one who is fully functional. The length of time the patient must be fully functional should be considered when defining remission. A patient could have 1 or 2 days of symptom-free functioning interspersed with days of severe and disabling anxiety symptoms, but to say that patient had 2 days of remission is meaningless. No published data clearly define a cutoff; one way to determine it may be to consider the likelihood of relapse or recurrence after a specific length of time. For example, if a patient is

From the Department of Psychiatry and Behavioral Sciences, Medical University of South Carolina, Charleston.

Presented at the symposium "Remission of Anxiety-Related Disorders," which was held October 6, 2000, in Washington, D.C., and supported by an unrestricted educational grant from Wyeth-Ayerst Laboratories.

Reprint requests to: James C. Ballenger, M.D., Department of Psychiatry and Behavioral Sciences, Medical University of South Carolina, 67 President St., P.O. Box 250861, Charleston, SC 29425.

Table 1. Remission of Panic Disorder^a

Option 1	Option 2
Essentially free of panic attacks No or mild agoraphobic avoidance No or minimal anxiety HAM-A score $\leq 7-10$	PDSS total score ≤ 3 , with no individual item score > 1
No functional impairment Sheehan Disability Scale score ≤ 1 (mildly disabled)	
HAM-D score ≤ 7	HAM-D score ≤ 7

^aBased on Ballenger.¹¹ Abbreviations: HAM-A = Hamilton Rating Scale for Anxiety, HAM-D = Hamilton Rating Scale for Depression, PDSS = Panic Disorder Severity Scale.

in remission for 3 months, is he or she less likely to become ill again? Another way would be to measure how long full functional recovery takes, i.e., how many months of doing well does it take for a patient to be back to living a normal life? If being free of symptoms and essentially well for 3 months is associated with a return to normal living in all aspects, then 3 months may be a sufficient guideline with which to define remission.

Another part of defining remission is related to medication dosage. A remitted patient should need no medication adjustments. He or she may choose to remain on continuation treatment, but no other changes in dose should be necessary.

It is useful to measure response in an objective way, preferably with a standardized test, and to have an objective and quantitative measure on which a clinician can base decisions such as changing medicines, raising doses, etc. In the treatment of people with anxiety disorders, using standardized tests would result in much easier practice, perhaps even much more successful practice, particularly in setting and realizing the goal of remission. Anxiety disorders should be treated to a standard, and that standard should be measured in ways that are both valid and easy to use. Using the above definition of remission, one standard would be to match the test scores of never-ill subjects. Each anxiety disorder should have its own objective criteria of remission, and proposed criteria for panic disorder, social anxiety disorder, GAD, OCD, and PTSD follow.

CRITERIA FOR REMISSION OF SPECIFIC ANXIETY DISORDERS

Panic Disorder

Proposed criteria for remission in panic disorder are presented in Table 1.¹¹ When defining criteria for remission for panic disorder, the clinician must be realistic, especially since the disorder is generally chronic with a high risk of relapse and recurrence.⁴ For example, one of the most frequently used criteria has been the absence of panic attacks, but, realistically, most former patients who become free of panic attacks remain panic free for weeks and months, but not on a constant basis. If a patient has 1 panic attack a year

and is doing well otherwise, then that patient could still be considered essentially free of panic attacks and meet this criterion for remission. Another example of the need for realistic goals is in agoraphobia. To treat agoraphobic avoidance until the patient is completely free of it in all circumstances is unrealistic and could potentially take a very long time or be impossible. A patient could be essentially well, yet, when faced with an unfamiliar situation such as flying on a rainy day, could revert to anxiety and avoidance. Such a reaction would not necessarily mean the patient's remission had ended. Remission goals of rare panic attacks, if any, and mild agoraphobic avoidance are more realistic than the absolute absence of such symptoms.

A third aspect of panic disorder is a free-floating anxiety that is present much of the time. The remission criterion, therefore, should be no or minimal anxiety, defined as a Hamilton Rating Scale for Anxiety (HAM-A)¹² score less than or equal to 7 to 10. Each of these cutoffs—7, 8, 9, and 10—works as an upper limit by which remission can be defined. The HAM-A is a 14-item clinician-rated instrument in which each item is rated from 0 (none) to 4 (severe, grossly disabling).

The fourth part of these remission criteria is no functional impairment. A Sheehan Disability Scale¹³ score of less than or equal to 1 on each item, which is described as mildly disabled, is a practical, easy score to use. This scale asks patients to score their disability in 3 areas—work, social life, and family life—from 0 (not at all) to 10 (extreme). It is always important to strike a balance between complexity and ease of use for both the patient and physician. The Sheehan scale has proved to be both valid and easy to use.

Depression is commonly comorbid with anxiety disorders, and the comorbidity of depression and panic disorder is one of the most often seen in psychiatry.¹⁴ Thus, the final criteria, which is present in all of these criteria for remission in anxiety disorders, is resolution of depression. A realistic guideline here is a 17-item Hamilton Rating Scale for Depression (HAM-D)¹⁵ score equal to or less than 7. Eight of the items on the clinician-rated HAM-D are scored 0 (not present), 1 (doubtful or trivial), or 2 (present); the other 9 are scored from 0 (not present) to 4 (severe). Therefore, a patient whose panic disorder is in remission is fully functional again, with perhaps a little anxiety or avoidance, and little to no depression.

In panic disorder, alternative ways of measuring symptoms are available. For example, a clinician could use the Panic Disorder Severity Scale¹⁶ instead of the HAM-A and Sheehan scales. This clinician-rated scale performs very well psychometrically, and it measures not only anxiety but frequency and severity of panic, agoraphobia, avoidance, and functional impairment in a single scale. It assesses 7 dimensions of panic disorder; each is scored from 0 (none) to 4 (severe). Remission has been defined as a score of 3 or less on this scale, with no individual item

Table 2. Remission of Social Anxiety Disorder^a

Core symptoms of social anxiety have disappeared
 LSAS score \leq 30
 No or minimal anxiety
 HAM-A score \leq 7–10
 No functional impairment
 Sheehan Disability Scale score \leq 1 (mildly disabled)
 HAM-D score \leq 7

^aBased on Ballenger.¹¹ Abbreviations: HAM-A = Hamilton Rating Scale for Anxiety, HAM-D = Hamilton Rating Scale for Depression, LSAS = Liebowitz Social Anxiety Scale.

Table 3. Remission of Generalized Anxiety Disorder^a

No or minimal anxiety
 HAM-A score \leq 7–10
 No functional impairment
 Sheehan Disability Scale score \leq 1 (mildly disabled)
 HAM-D score \leq 7

^aBased on Ballenger.¹¹ Abbreviations: HAM-A = Hamilton Rating Scale for Anxiety, HAM-D = Hamilton Rating Scale for Depression.

score above 1.¹⁷ The HAM-D would still need to be used to measure depressive symptoms. Either of these options of measuring symptoms and defining remission in patients with panic disorder is a valid one.

Social Anxiety Disorder

The field of social anxiety disorder has been dominated by one scale, the Liebowitz Social Anxiety Scale (LSAS).¹⁸ In addition to its use in research, this scale can easily be used in clinical practice to track social anxiety. The LSAS forces the clinician to ask a series of questions in a fairly comprehensive look at possible social anxiety symptoms. It rates 24 potentially anxiety-producing situations in both severity of fear and anxiety (0 = none to 3 = severe) and frequency of avoidance (0 = never to 3 = usually). Its comprehensive nature provides a broad measure of severity, and it is very useful in following improvement with treatment.

Severe scores on the LSAS are in the 80 to 120 range. A third of patients in recent studies have scored in the severe range. Moderate severity is signified by scores from 60 to 80, and mild, from 40 to 60. For remission, patients should score 30 or below (Table 2).¹¹ This cutoff is appropriate for 2 reasons: first, it is clinically significantly separate from the mild range of 40 to 60, so it seems right conceptually. Second, data exist that support the use of 30 as a cutoff. Heimberg and colleagues¹⁹ analysis found that scores of healthy patients and those of patients with social anxiety disorder separated at 30 with good sensitivity and specificity.

The other 3 criteria for remission of social anxiety disorder could be the same as those for panic disorder. People with social anxiety disorder should not only lose their avoidance and phobia of social situations, but they also should have minimal and infrequent anxiety in anticipa-

Table 4. Remission of Obsessive-Compulsive Disorder^a

No or minimal obsessions or compulsions
 Y-BOCS score \leq 8
 No or minimal anxiety
 HAM-A score \leq 7–10
 No functional impairment
 Sheehan Disability Scale score \leq 1 (mildly disabled)
 HAM-D score \leq 7

^aAbbreviations: HAM-A = Hamilton Rating Scale for Anxiety, HAM-D = Hamilton Rating Scale for Depression, Y-BOCS = Yale-Brown Obsessive Compulsive Scale.

tion of those situations. Again, a HAM-A score less than or equal to 7 to 10 and a Sheehan Disability Scale score less than or equal to 1 are among the suggested criteria for remission, as is a HAM-D score less than or equal to 7. Depression is frequently comorbid with social anxiety disorder—40% to 50% of patients have this comorbidity, and up to 55% of those have suicidal ideation.⁵ With the scores specified here, a patient with social anxiety disorder should have few symptoms, a return to function, and little to no depression. These criteria may seem demanding, but it is better to err on the side of having stringent criteria to encourage clinicians and patients to be appropriately aggressive with treatment.

Generalized Anxiety Disorder

As shown in Table 3,¹¹ the criteria for GAD are the same as the last 3 criteria for social anxiety disorder: HAM-A score less than or equal to 7 to 10, Sheehan Disability Scale score no greater than 1, and a HAM-D score less than or equal to 7. These criteria depend heavily on the HAM-A, which is a less-than-perfect measure in both the research and clinical arenas. Shorter versions that concentrate mainly on the first 2 items—worry and tension—are being tested, but have yet to be fully validated. Currently, though, the HAM-A remains the best option to measure GAD symptoms.

Obsessive-Compulsive Disorder

As in social anxiety disorder, study of OCD is dominated by a single scale, in this case, the Yale-Brown Obsessive Compulsive Scale (Y-BOCS).²⁰ The Y-BOCS is like the Panic Disorder Severity Scale and the LSAS in that it tries to comprehensively measure all of the obsessions and compulsions of OCD, and it results in a score that reflects the entire syndrome. This clinician-rated scale has 10 items, each scored from 0 (none) to 4 (extreme). A score of 8 or below signals remission (Table 4). Some might argue that a score anywhere from 8 to 16 would work as a cutoff for remission, but since the bottom level for entry into clinical trials is often 16, using a score higher than an 8 is probably too high. For example, Eisen et al.⁷ reported a mean baseline score of 21 in their subjects and used a score of 16 or higher to define the presence of OCD. A score of 16 reflects moderately severe

Table 5. Remission of Posttraumatic Stress Disorder PTSD^a

No or minimal PTSD symptoms TOPS-8 score \leq 5 or 6
No or minimal anxiety HAM-A score \leq 7–10
No functional impairment Sheehan Disability Scale score \leq 1 (mildly disabled) HAM-D score \leq 7

^aAbbreviations: HAM-A = Hamilton Rating Scale for Anxiety, HAM-D = Hamilton Rating Scale for Depression, TOPS-8 = Treatment Outcome PTSD Scale.

symptoms, 12 to 16 reflects milder symptoms, and 8 to 12, even milder. Therefore, a score less than or equal to 8 on the Y-BOCS seems to be a reasonable criterion.

Again, the last 3 criteria can be the same as those used in the other anxiety disorders: a HAM-A score less than or equal to 7 to 10, a Sheehan Disability Scale score less than or equal to 1, and, again, because OCD and depression are often comorbid, a HAM-D score less than or equal to 7. Scores in these ranges would document that a patient is well and in remission.

Posttraumatic Stress Disorder

PTSD, the fifth anxiety disorder to be discussed, is a very common disorder. Breslau et al.²¹ found that about 1 in 10 of those interviewed who had experienced trauma developed PTSD, and 1 in 5 who had been victims of assaultive violence—rape, mugging, combat, and so on—developed PTSD. When one considers that PTSD is a possible result of events such as inner-city violence and motor vehicle accidents—both have an extremely high prevalence rate—and rape and natural disasters, as well as combat, it should not be surprising that current lifetime prevalence estimates are as high as 8% and higher.²²

The principal measure of PTSD symptoms proposed here is, again, a comprehensive questionnaire-type scale like the Panic Disorder Severity Scale and the Y-BOCS: the 8-item Treatment Outcome PTSD Scale (TOPS-8).²³ The TOPS-8 is a recently developed clinician-rated scale that is shorter and easier to use than the Clinician Administered PTSD Scale (CAPS),²⁴ but is highly correlated with the CAPS. It rates 8 dimensions of PTSD from 0 (none or no problem) to 4 (extremely severe). The CAPS takes so much time and energy of the patient and clinician to administer that recent research trials are moving away from it; those features also make it impractical for use in private practice. The TOPS-8 can be conducted fairly rapidly and results in a score that accounts for the full range of PTSD symptom clusters—reexperiencing/intrusion, avoidance/numbing, and hyperarousal. A score of 5 or less on the TOPS-8 reflects no or minimal PTSD symptoms and is an appropriate upper limit for remission (Table 5). A score of 7 still reflects mild symptoms; 15, moderate symptoms; 18, marked symptoms; and 21, severe symptoms. Only patients with very mild or no symptoms would

score a 5 (or perhaps a 6) on the TOPS-8. The other criteria for remission of PTSD would be the same, i.e., HAM-A score less than or equal to 7 to 10, Sheehan Disability Scale score less than or equal to 1, and HAM-D score less than or equal to 7.

DISCUSSION

The principal goals of setting these remission criteria are to set the standards high but find realistic criteria that are not only valid but practical for clinical use. It is valuable to keep the goals high because that encourages both the physician and the patient to document progress carefully, track which treatments work and which do not, and change treatment if necessary to reach the goal of remission. Using instruments to yield an objective measure when treating patients with psychiatric disorders helps the clinician clarify when treatment should be intensified or changed and when functional recovery and remission have been achieved. However, using these criteria realistically is important. Trying to completely eliminate anxiety is asking too much, since mild anxiety is common and often normal. Instead, the goal is for there to be almost no symptoms and full function.

The use of a 3-month observation period to determine if a patient who is doing well is in remission gives the doctor and patient a specific time at which they can move into a different kind of treatment. In the anxiety disorders, hopefully few patients will discontinue medication altogether after only 3 symptom-free months, since current data show that continued medication treatment can protect against relapse.^{4,8,25,26} However, the intensity of other types of treatment may merit reconsideration. For example, a clinician may decide that he or she needs to see a remitted patient only every 6 months instead of more frequently. The use of these criteria tells the doctor and patient when the need for acute, active treatment ends and maintenance treatment begins.

The anxiety disorders in general do not remit spontaneously. Once they become established, they are usually chronic, lifelong conditions that merit long-term pharmacologic treatment. Since the economic cost and personal burden of anxiety disorders are both so high, the clinician should treat patients with these disorders to remission—in other words, continuing suitably aggressive treatment until the patients are indistinguishable from never-ill counterparts. This is a high and stringent standard, but anything short of that goal is unfair to both clinician and patient. The use of standardized measures like the ones suggested here provides an objective way to evaluate treatment response, define remission, and guide treatment appropriately.

Disclosure of off-label usage: The author has determined that, to the best of his knowledge, no investigational information about pharmaceutical agents has been presented in this article that is outside U.S. Food and Drug Administration–approved labeling.

REFERENCES

1. Frank E, Prien RF, Jarrett RB, et al. Conceptualization and rationale for consensus definitions of terms in major depressive disorder. *Arch Gen Psychiatry* 1991;48:851–855
2. Judd LL, Paulus MP, Wells KB, et al. Socioeconomic burden of subsyndromal depressive symptoms and major depression in a sample of the general population. *Am J Psychiatry* 1996;153:1411–1417
3. Melfi CA, Chawla AJ, Croghan TW, et al. The effects of adherence to antidepressant treatment guidelines on relapse and recurrence of depression. *Arch Gen Psychiatry* 1998;55:1128–1132
4. Pollack MH, Smoller JW. The longitudinal course and outcome of panic disorder. *Psychiatr Clin North Am* 1995;18:785–801
5. Ballenger JC, Davidson JRT, Lecrubier Y, et al. Consensus statement on social anxiety disorder from the International Consensus Group on Depression and Anxiety. *J Clin Psychiatry* 1998;59(suppl 17):54–60
6. Yonkers KA, Warshaw MG, Massion AO, et al. Phenomenology and course of generalised anxiety disorder. *Br J Psychiatry* 1996;168:308–313
7. Eisen JK, Goodman WK, Keller MB, et al. Patterns of remission and relapse in obsessive-compulsive disorder: a 2-year prospective study. *J Clin Psychiatry* 1999;60:346–351
8. Ballenger JC, Davidson JRT, Lecrubier Y, et al. Consensus statement on posttraumatic stress disorder from the International Consensus Group on Depression and Anxiety. *J Clin Psychiatry* 2000;61(suppl 5):60–66
9. Greenberg MA, Sisitsky T, Kessler RC, et al. The economic burden of anxiety disorders in the 1990s. *J Clin Psychiatry* 1999;60:427–435
10. Haskins JT. Generalized anxiety disorder: epidemiology, impact of comorbidity, and natural history. *Postgrad Med Special Report* 1999;3–9
11. Ballenger JC. Clinical guidelines for establishing remission in patients with depression and anxiety. *J Clin Psychiatry* 1999;60(suppl 22):29–34
12. Hamilton M. The assessment of anxiety states by rating. *Br J Med Psychol* 1959;32:50–55
13. Leon AC, Shear MK, Protera L, et al. Assessing impairment in patients with panic disorder: the Sheehan Disability Scale. *Soc Psychiatry Psychiatr Epidemiol* 1992;27:78–82
14. Ballenger JC. Comorbidity of panic and depression: implications for clinical management. *Int Clin Psychopharmacol* 1998;13(suppl 4):S13–S17
15. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry* 1960;23:56–62
16. Shear MK, Brown TA, Barlow DH, et al. Multicenter Collaborative Panic Disorder Severity Scale. *Am J Psychiatry* 1997;154:1571–1575
17. Shear MK, Clark D, Feske U. The road to recovery in panic disorder: response, remission, and relapse. *J Clin Psychiatry* 1998;59(suppl 8):4–8
18. Liebowitz MR. Social phobia. *Mod Probl Pharmacopsychiatry* 1987;22:141–173
19. Heimberg RG, Horner KJ, Juster HR, et al. Psychometric properties of the Liebowitz Social Anxiety Scale. *Psychol Med* 1999;29:199–212
20. Goodman WK, Price LH, Rasmussen SA, et al. The Yale-Brown Obsessive Compulsive Scale. *Arch Gen Psychiatry* 1989;46:1006–1016
21. Breslau N, Kessler RC, Chilcoat HD, et al. Trauma and posttraumatic stress disorder in the community: the 1996 Detroit Area Survey of Trauma. *Arch Gen Psychiatry* 1998;55:626–632
22. Kessler RC, Sonnega A, Bromet E, et al. Posttraumatic stress disorder in the National Comorbidity Study. *Arch Gen Psychiatry* 1995;52:1048–1060
23. Davidson JR, Colket JT. The eight-item treatment-outcome post-traumatic stress disorder scale: a brief measure to assess treatment outcome in post-traumatic stress disorder. *Int Clin Psychopharmacol* 1997;12:41–45
24. Blake DD, Weathers FW, Nagy LM, et al. A clinician rating scale for assessing current and lifetime PTSD: the CAPS-1. *Behav Therapist* 1990;13:187–188
25. Davidson JRT. Pharmacotherapy of social anxiety disorder. *J Clin Psychiatry* 1998;59:47–53
26. Rasmussen SA, Eisen JL. Treatment strategies for chronic and refractory obsessive-compulsive disorder. *J Clin Psychiatry* 1997;58(suppl 13):9–13