Measuring Outcome in Posttraumatic Stress Disorder

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This article summarizes the features of posttraumatic stress disorder (PTSD) that may affect treatment outcome and discusses the areas in which treatment outcome can be productively evaluated. PTSD is a complex psychiatric condition that tends to run a chronic course. Measurement of treatment outcome in PTSD is confounded by multiple factors, including a high prevalence of comorbid disorders, reactivation of the syndrome by ongoing environmental stressors, spontaneous recovery of the early disorder, and a fluctuating course of the chronic disorder. Four principal domains of treatment outcome may be evaluated in PTSD: core symptom severity, comorbid conditions (particularly depression), adverse practices (e.g., violence or alcohol consumption), and social/vocational disability. To gain an accurate assessment of these domains, a comprehensive assessment battery is needed. The relevant instruments and their yield in studies of PTSD are reviewed.

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P osttraumatic stress disorder (PTSD) is one of the few psychiatric disorders for which the onset of the chronic stage is formally defined: chronic PTSD is diagnosed in individuals who express the syndrome for 3 months. This time lag is shorter than those used to define chronicity in other chronic psychiatric disorders, and its choice may reflect a widespread and erroneous view that PTSD quickly becomes unremitting and resistant to change.

The negative results of the first treatment studies, most of which concerned patients who had had PTSD for decades, may have created this view.^{1,2} Inaccurate measurements of treatment effect may have further reinforced such early impressions. For example, some of the earlier rating scales for PTSD evaluated incomplete sets of symptoms (e.g., the original version of Horowitz's Impact of Event Scale³ did not measure symptoms of hyperarousal). Moreover, we know now that not all PTSD symptoms are equally amenable to change.⁴ Finally, treatment effect in PTSD may become apparent only after longer periods of time than those used in treatment studies.

This is not to say that measuring outcomes in PTSD is easy. In psychiatry, assessments are mostly performed in the context of a specific question. Reducing reality to selected and measurable components, however, will ultimately affect outcome. In PTSD particularly, outcome measurements that are limited to core PTSD symptoms (reexperiencing, avoidance, and hyperarousal) may not capture other clinically relevant effects of treatment. For example, a remission of comorbid syndromes, such as depression and alcohol abuse, has important clinical implications that may escape a narrow approach to measuring outcome. Similarly, the effect of treatment on impairment and disability (e.g., social avoidance, low tolerance of frustration) can not be directly derived from change in symptoms. Adverse living conditions, ongoing traumatization, and exposure to reminders of the traumatic event can confound the effect of treatment and should be monitored as well.⁵

In this article, the following questions related to the assessment of improvement in patients with PTSD are addressed: What are the clinically relevant features of PTSD, beyond its syndromal definition by DSM-IV⁶? What are the confounding factors to measurement of such features? What are the relevant targets for treatment? What instruments are available to facilitate the evaluation of treatment outcome? How did these instruments fare in previous studies of PTSD?

MEASURING TREATMENT EFFECT

What Are the Pertinent Features of PTSD?

As currently defined, PTSD itself consists of a complex combination of co-occurring symptoms and mental processes. PTSD symptoms of anxious avoidance have been linked with biological mechanisms of fear conditioning and harm avoidance.⁷ Intrusive and distressful recollections of the traumatic event have been previously described in acute grief⁸ and may be related to elements of loss and separation. Loss of interest in pleasurable activities and sense of foreshortened future are clearly depres-

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Figure 1. Anxiety, Depression, and Posttraumatic Stress Disorder (PTSD) 4 Months After Trauma^a

sive symptoms. Hypervigilance and hyperarousal, as well as impaired cognitive function (which may even precede the traumatic event⁹), may also be independent dimensions of this disorder.

Beyond PTSD symptoms, other clinically relevant phenomena are often associated with the disorder. Among the better studied is the association between PTSD and major depression. According to the National Comorbidity Survey (NCS), a community-based study of more than 5800 individuals, 7.8% of the population will experience PTSD at some point in their lives.¹⁰ Almost half of these individuals will experience depression at the same time. Figure 1 shows the results of a prospective evaluation of 211 trauma survivors 4 months after the initiating event,¹¹ demonstrating that even at this early stage, more than 40% of the patients who met DSM-III-R criteria for PTSD also had major depression. Moreover, depressive symptoms, seen early on after traumatization, are powerful predictors of the development of chronic PTSD.12 The high prevalence of comorbid depression in PTSD has, therefore, important implications for the expected outcome of treatment in PTSD.

Another accompanying feature of PTSD is affective dyscontrol, expressed both as numbing and detachment and as bursts of anger and violence. Low tolerance of frustration in PTSD may lead to difficulties in sustaining stable employment, to marital strife, and to troubles with the law. Improvement in impulse control is, therefore, an important, independent, and achievable goal of treatment. For example, in an analysis of the outcome of a 4-month intensive inpatient program for combat-related PTSD among Vietnam veterans, Johnson et al.¹³ found a decrease in violent actions and thoughts and in legal problems. Paradoxically, these results were associated with an increase in PTSD symptoms from admission to follow-up. Patients' evaluations similarly indicated that the most desirable effects of the treatment program were improved morale and interpersonal relationships.

Biased stimulus recognition,¹⁴ difficulties in discriminating threatening stimuli from innocuous ones, and impaired habituation of autonomic responses to loud tones¹⁵ represent other clinically relevant phenomena. Often unbeknown to the patient, these implicit features of PTSD may lead to inappropriate vigilance, arousal, and irritability. Intolerance of intense stimuli is probably behind much of the avoiding lifestyle led by some PTSD patients and thereby behind their social isolation and alienation.

Finally, PTSD is often associated with misuse of psychotropic agents, including prescribed medication, illicit substances, and alcohol. PTSD patients are also prone to engage in risky behavior (e.g., excess mortality among PTSD patients has been attributed to violent causes of death).¹⁶ An indirect result of proper therapy for PTSD may be a reduction in such adverse health practices.

An improvement in PTSD patients' health status may, therefore, be expressed in many different ways. Importantly, core PTSD symptoms may not be the first ones to respond to treatment, and some may not respond at all. Intrusive and distressful recall of traumatic events, for example, can be found in trauma survivors regardless of the presence of PTSD (e.g., in up to 91% of holocaust survivors).¹⁷ Several PTSD programs have reported improvement on "auxiliary" symptoms and interpersonal behavfor^{3,13,18} The assessment of treatment effect in PTSD should therefore be comprehensive and inclusive.

What Are the Confounding Factors?

The measurement of PTSD symptoms may be confounded by 3 major factors: (1) nonspecific and uncontrolled effect of treatment interventions, (2) intercurrent environmental demands on the patient, and (3) factors related to the natural course of the disorder.

First among the nonspecific effects of treatment is the often-observed placebo effect. Being enrolled in a standardized treatment program, being given attention, and being given a pill are powerful modulators of one's feelings. Moreover, the patient's appraisal of his or her symptoms may be affected by being asked about them time and again during assessment sessions of a drug trial. In PTSD, the action of being repeatedly interviewed about one's trauma and the ensuing feelings may, indeed, simulate the effect of desensitizing exposure. Given the frequent use of selfreport instruments in psychiatry, a change in selfevaluation will significantly affect the reported effect of treatment.

Other confounds related to enrolling patients in a treatment study are related to sampling bias and patient selection. For example, PTSD patients who are not receiving psychotropic medication or who can discontinue current treatment without major negative effects may not represent the population of patients regularly seen in psychiatric clinics. Similar sampling bias may occur when patients are selected on the basis of presence (or absence) of comorbid disorders. Keeping a detailed record and an initial evaluation of patients who are subsequently excluded from a study can identify potential selection bias.

Importantly, the expression of PTSD symptoms is extremely sensitive to ongoing environmental demands, particularly to events and situations that resemble the original traumatic experience. The presence of negative life events, ongoing traumatization, or harsh living conditions may negatively affect the results of treatment studies.^{2,5} This is particularly true for study participants who continue to live in a high-risk environment, such as inner cities or war-prone areas of the world. Monitoring the presence and severity of ongoing stressors during treatment studies makes a lot of sense.

Despite the comparable expression of PTSD across traumatic events, the severity and duration of the traumatic event and the age at which it occurred may affect the response to treatment. Patients who have suffered from prolonged traumatizations (e.g., captivity and torture) or from early-life adversities (e.g., child abuse) may differ from those meeting the same PTSD diagnostic criteria whose syndrome has followed shorter events (e.g., road traffic accidents). The underlying biological mechanisms of exposure to prolonged or repeated traumatiza tion (e.g., surrender and exhaustion) may differ from that of acute traumatization (mostly fear), and such differ ences may affect the response to treatment. There is preliminary evidence that PTSD that has resulted from a more recent event may have a better treatment response than complex and chronic PTSD¹⁹; however, this area has not received enough attention and is worthy of further study.

Complicating matters further, some patients may have partial or subsyndromal forms of PTSD²⁰ yet show a substantial degree of disability.²¹ Moreover, formal recovery from PTSD (i.e., not meeting the full criteria for PTSD) is often confounded with losing only the avoidance element of the syndrome, while intrusive memories and hyperarousal may remain. Claims in treatment studies of inducing "recovery" from PTSD should therefore be tested against the specific nature of such recovery.

Finally, the course of PTSD is often fluctuating and unstable. Spontaneous recovery occurs in more than 60% of patients with recent PTSD between 1 and 6 years after trauma.¹⁰ This poses a problem of attributing an improvement to the specific effect of treatment. In order to address this problem, treatment studies should optimally include patients at a similar stage of their response to trauma. Chronic PTSD may also run a fluctuating course, as shown by a change of up to 50% in individual symptom intensity occurring between 2 measurement sessions.²² Figure 2 demonstrates the spontaneous fluctuations of



^aData from Niles et al.²² The horizontal bar in each Time column designates the mean Mississippi Scale for Combat-Related Posttraumatic Stress Disorder (MISS) score for all subjects. ^bOne year after Time I. ^cValues shown are percent changes in MISS score for each patient.

PTSD symptoms (Mississippi Scale for Combat-Related Posttraumatic Stress Disorder [MISS] total scores) in a population of veterans from the Vietnam War. Interestingly, the group mean MISS score remained constant, while individual scores showed large variation. The origin of such fluctuations is unknown, and they might be related to the above mentioned environmental stressors.

Defining Relevant Targets for Treatment

Areas of potential interest include PTSD symptoms, comorbid disorders, associated behavior, disability, and quality of life. PTSD symptoms are the first obvious target for treatment, but it is unclear whether all or just some symptoms should be measured. Some symptoms are more likely to change with treatment, and specific rating scales, described later in this review, have been developed for this purpose. A broad global assessment of severity is a third option for measuring treatment effects.

Among PTSD symptoms, insomnia and uncontrolled anger are of particular impact on the patient's life and may respond to specific treatment (e.g., mood stabilizers in the case of anger and irritability).^{23,24} Avoidance in PTSD includes both fearful avoidance of trauma-related cues and recollection and generalized avoidance of social situations and avoidant lifestyle. These different facets of avoidance may be targeted by specific treatment interventions (e.g., exposure for specific avoidance and social skills groups for generalized avoidance). Finally, the presence of dissociative symptoms is often particularly troublesome and worth addressing in therapy. More often than not, PTSD is accompanied by major depression.^{10,11,25} Importantly, depression and anxiety may lead to suicidal behavior in PTSD.^{26,27} Improvement in depressive symptoms may or may not follow that of PTSD symptoms, hence the need to monitor these 2 symptom domains independently.

Associated behavior patterns are difficult to measure. Substance abuse, isolation, violence, and impaired social and interpersonal function are dimensions of PTSD that are not "formal" symptoms but are extremely disturbing for the patient and his or her environment. As mentioned above, there is some evidence that these associated behaviors may be as reactive to treatment as much as some "core" PTSD symptoms. Moreover, specific treatment interventions may target each of these areas. Disability and quality of life are other areas of interest for which generic rating scales are widely available.

Beyond choosing an appropriate dimension to measure, a gauge of the expected efficacy of the intervention is often desirable. The length and the impact of previous treatment trials is an important factor to consider when planning a treatment study in PTSD. PTSD is a chronic disorder, and many patients would previously have been in treatment when entering a novel study. Treatment resistance, however, has not been properly defined in PTSD. Yet, as we know all too well, many PTSD patients have failed to improve in several trials of various pharmacologic and nonpharmacologic therapies. Recognizing treatment resistance is particularly important because it may lead to enlightened use of augmentation techniques, such as the ones used in other mental disorders. Knowledge of the expected effect size of therapies in PTSD may also lead to predefining criteria for success and failure in the treatment of specific patient populations.

INSTRUMENTS USED TO ASSESS PTSD

Table 1 lists instruments that have been used in previous clinical studies of PTSD. The list is not meant to be comprehensive, but rather to point to directions in evaluating the severity of the disorder and treatment outcome. The rating scales can be divided into those that determine PTSD diagnostic status, those that assess PTSD symptoms, those that make global clinical assessments, and scales that rate the severity of associated conditions, level of disability, and quality of life.

PTSD and Comorbid Disorders: Formal Diagnoses

Accurate diagnosis of PTSD is a sine qua non for conducting treatment studies. The Structured Clinical Interview for DSM-IV (SCID-IV)²⁸ is the ex officio structured clinical interview for DSM-IV Axis I disorders. The SCID-IV yields detailed diagnoses of PTSD and comorbid disorders, current and lifetime. The algorithmic and modular structure of the SCID-IV allows for quick exclusion of

Table 1. Rating Scales for Use in Studies of PTSD				
Evaluation	Assessor			
Diagnosis of PTSD				
Structured Clinical Interview for DSM-IV (SCID-IV)	Clinician			
Clinician Administered PTSD Scale (CAPS)	Clinician			
Posttraumatic Diagnostic Scale (PTDS)	Patient			
PTSD symptoms				
Clinician Administered PTSD Scale (CAPS)	Clinician			
Posttraumatic Diagnostic Scale (PTDS)	Patient			
Impact of Event Scale (IES)	Patient			
Davidson Trauma Scale (DTS)	Patient			
Mississippi Scale for Combat-Related				
Posttraumatic Stress Disorder (MISS)	Patient			
Treatment-Outcome PTSD scale (TOP-8)	Clinician			
Global clinical assessment				
Clinical Global Impressions scale (CGI)	Clinician			
Severity of Illness scale	Clinician			
Global Improvement scale	Clinician			
Duke Global Rating of PTSD (DGRP)	Clinician			
Comorbid disorders and symptoms				
Structured Clinical Interview for DSM-IV (SCID-IV)	Clinician			
Dissociative Experiences Scale (DES)	Patient			
Beck Depression Inventory (BDI)	Patient			
Montgomery-Asberg				
Depression Rating Scale (MADRS)	Clinician			
Spielberger State-Trait Anxiety Inventory (STAI)	Patient			
Hamilton Rating Scale for Depression (HAM-D)	Clinician			
Hamilton Rating Scale for Anxiety (HAM-A)	Clinician			
Disability and vulnerability to stress				
Global Assessment of Functioning (GAF)	Clinician			
Sheehan Disability Scale	Patient			
Sheehan Vulnerability to Stress (VS) scale	Patient			
Quality of life				
Quality of Life Enjoyment and				
Satisfaction Questionnaire (Q-LES-Q)	Clinician			
<u>^</u>				

disorders that are not present. It is also possible to use portions of the SCID-IV to evaluate one or more pertinent disorders' (e.g., PTSD, depression, other anxiety disorders). The instrument includes a thorough evaluation of alcohol and substance misuse disorders. The SCID-IV has to be administered by trained clinicians and requires clinical judgment and experience. The main advantage of using the SCID-IV in studies of PTSD is the instrument's ability to detect concurrent (comorbid) disorders. The SCID-IV does not evaluate the severity of mental disorders.

The Clinician Administered PTSD Scale (CAPS)^{29,30} is a structured clinical interview dedicated to PTSD. The CAPS has been widely used in clinical studies of PTSD, including treatment studies. The CAPS examines all 3 symptom clusters of PTSD, quantifying symptom frequency and intensity for each PTSD symptom during the past month or past 2 weeks, depending on the version used. The CAPS yields both a continuous measure of symptom severity and a dichotomous diagnosis of PTSD. As with the SCID-IV, the administration of the CAPS requires clinical skills, judgment, and experience. The CAPS has been used effectively to evaluate change in symptom intensity over time.

Complementing these 2 structured clinical interviews, the Posttraumatic Diagnostic Scale (PTDS)³¹ is a selfreport measure of posttraumatic stress disorder that yields both a diagnosis of PTSD and a measure of PTSD symptom severity. The instrument's items follow DSM-IV diagnostic criteria for PTSD and ask about symptoms expressed during the past month. The PTDS also addresses the nature of the stressful event, the duration of the disturbance, and the resulting impairment. It contains, therefore, all the required criteria for making the diagnosis of PTSD. The instrument has been validated against the SCID and was found to have good sensitivity and specificity. Its time resolution (1 month) should be considered when planning for repeated assessment sessions.

PTSD: Symptom Severity

The Impact of Event Scale (IES)³ is arguably the oldest and the most widely used self-report rating scale of trauma-related symptoms. Although it does not strictly follow DSM diagnostic criteria, the IES does evaluate the 3 main symptom domains, intrusion, avoidance, and hyperarousal.³² The IES quantifies 22 current (past week) symptoms, each on a severity rating of 0 to 5, and is fairly sensitive to changes in symptoms between 2 timepoints. The IES yields a total score but can also be subdivided into 3 subscales, corresponding to the above-mentioned symptom domains. The factor structure of the IES is indeed robust and has been shown to be consistent across studies.⁵ The IES has been translated into many languages and validated in several studies.³³ It has been used extensively in treatment studies.

The Davidson Trauma Scale (DTS), a 17-item clinity cian-administered scale, is a self-report instrument that measures both the frequency and severity of each DSM-IV PTSD symptom.³⁴ The DTS has been shown to have good predictive properties for response to treatment and is sensitive to treatment effect.

Finally, the Mississippi Scale for Posttraumatic Stress Disorder³⁵ is a 35-item self-report questionnaire that focuses on the symptomatology found specifically after trauma. The MISS has both civilian³⁶ and combat-related versions. It does not follow DSM-IV symptoms yet has been used in numerous epidemiologic studies of PTSD from which a cutoff score has been derived to define "caseness" (i.e., the presence or absence of PTSD).

PTSD: Selected Symptoms

There are 2 approaches to measuring selected symptoms in drug trials. One is to evaluate change in specific symptom domains, such as intrusion or avoidance. The other is to evaluate symptoms that are more likely to be affected by treatment. The first approach uses one or several parts of a PTSD rating scale, such as the intrusion or avoidance subscales of the IES. The second approach is exemplified by Davidson's 8-item treatment-outcome PTSD scale (TOP-8).⁴ The TOP-8 is a brief interview based on 8 PTSD symptoms that have been shown to respond well to treatment interventions. It was developed from a larger (19-item) PTSD evaluation scale (the Structured Interview for PTSD [SI-PTSD]³⁷) by selecting items that occur frequently in patients with PTSD and respond well to treatment. The 8 items belong to all 3 symptom clusters for PTSD and have been shown to detect drug/ placebo differences better than the original scale. The TOP-8 has been shown to correlate significantly with a self-rated measure of PTSD and can distinguish between responders and nonresponders on the Clinical Global Impressions scale (CGI).

Global Measures of Improvement

Clinical observation may capture dimensions of behavior that are not readily reduced to specific symptoms. Global assessment scales quantify such observations. The most widely used is the CGI.³⁸ The CGI asks the clinician to refer to his or her "total clinical experience" to assess the severity of the patient's current mental illness (1 item) and to evaluate improvement from the patient's baseline condition as previously observed (1 item). The CGI, therefore, captures and quantifies a global impression by the clinician regarding both severity and improvement. It offers a crude, yet very useful measure of change in patients with mental disorders that can be used across disorders and in states of high comorbidity. The CGI has been used extensively to provide outcome measures in treatment studies of PTSD, depression, and anxiety disorders.

Specifically designed for PTSD, the Duke Global Rating of PTSD (DGRP) offers a global evaluation of PTSD by an observing clinician. As does the CGI, the DGRP refers to the clinician's "total clinical experience with this particular population" as a basis for a global evaluation of 4 items: intrusive phenomena, avoidant behavior, hyperarousal, and overall severity. Each item is rated on a severity scale of 1 to 7.

Comorbid Disorders and Associated Symptoms

Depression, anxiety, and dissociation are among the most frequently evaluated comorbid symptoms in PTSD. Dissociative symptoms may be evaluated using the Dissociative Experience Scale (DES),³⁹ although this instrument is rather long and not specifically designed to evaluate change over time.

Improvement in symptoms of anxiety and depression is often, yet not always, associated with improvement in PTSD symptoms. There are several widely used instruments that allow an evaluation of depressive symptoms and anxiety in PTSD (e.g., the Beck Depression Inventory [BDI],⁴⁰ the Montgomery-Asberg Depression Rating Scale [MADRS],⁴¹ the Spielberger State-Trait Anxiety Inventory [STAI]).⁴² The use of these measures in studies of PTSD is recommended since they capture frequent features of the clinical syndrome that the "pure" PTSD scales do not. The Hamilton Rating Scale for Depression (HAM-D)⁴³ and Hamilton Rating Scale for Anxiety (HAM-A)⁴⁴ have been widely used in clinical studies of PTSD.

Disability and Vulnerability to Stress

Included in the SCID-IV is a revised Global Assessment of Functioning scale (GAF). The GAF adapts a numeric score (on a scale of 10-100) to levels of personal and social functioning that are described verbally in the instrument. As part of the SCID, this scale is designed to be used across mental disorders and to capture all levels of disability, from chronic hospitalization with care for daily activities to undisturbed functioning in the community. The GAF is not syndrome specific and therefore may be used in the presence of complex comorbid psychopathology.

Used in drug studies of PTSD and other mental disorders, the Sheehan Disability Scale45 is a self-report instrument (3 items, rated 1-10) used to assess the degree to which mental symptoms have disrupted the patient's work, social life, and family/home responsibilities. An additional stress and social support scale (also referred to as "Vulnerability to the Effect of Stress," or VS⁴⁶) addresses the degree to which co-occurring stressors could interfere with one's work, leisure, social, health, and financial situations (1 global item scored 1-10) and the degree of support received from others, relative to needs, during the past week (1 item, identical).

Quality of Life

uality of Life Improvements in the patient's quality of life is what treatment is, ultimately, trying to achieve. Quality of life has been defined in different ways, and many instruments have been derived from such definitions, mostly for use in basic research and epidemiologic studies. The effect of treatment of PTSD on quality of life has been evaluated using Endicott's Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q).47,48 The Q-LES-Q is a selfreport measure designed to investigate the degree of enjoyment and satisfaction experienced by subjects in various areas of daily functioning. In the above-mentioned study, this instrument was shown to be sensitive to treatment effects (Table 2).

Rating Scales in Practice

This last section addresses the usefulness of rating scales from another perspective: it looks at the degree to which rating instruments were able to differentiate active treatment from placebo effect in previous clinical trials. The results from treatment studies using various PTSD rating scales are presented in Table 2. The difference in response rate between active study drug and placebo and the ratio between these response rates give an indication of the amount of the active drug's effect that can be accounted for by a placebo response. With the majority of PTSD rating scales used in these studies, up to two thirds of the active treatment response could be attributed to placebo re-

Table 2. Active Dru	g/Placebo	Response	Rates	Using	PTSD
Rating Scales	-	-		-	

	Mean Improvement, % of Patients		Drug/	
	Active		Placebo	
Rating Scale	Drug	Placebo	Ratio	Reference
IES total	47	19	0.40	Davidson et al49
IES total	65	28	0.43	Kosten et al50
IES total	68	25	0.37	Kosten et al50
CAPS total	60	40	0.67	Baker et al ⁵¹
CAPS total	52	29	0.56	Katz et al ⁵²
CGI	85	62	0.73	van der Kolk et al ¹⁹
IES intrusion	53	35	0.66	Davidson et al53
IES avoidance	47	35	0.72	Davidson et al53
CAPS				
avoidance	47	34	0.72	Davidson et al53
CAPS				
occupation	47	25	0.53	Davidson et al53
DTS	43	27	0.63	Davidson et al53
DTS	39	24	0.62	Brady et al ⁴⁸
Q-LES-Q	22	6	0.27	Brady et al ⁴⁸

sponse. Importantly, significant treatment/placebo effect has been shown for most area studies, including symptom severity, global evaluation of outcome, quality of life, and vulnerability to stress. These data demonstrate the usefulness of comprehensive evaluation of outcome in treatment studies of PTSD.

what As shown in this brief overview, some PTSD symp-and in trauma survivors without PTSD and in functionally remitted PTSD patients. When designing strategies to measure PTSD outcome, it is essential to remember that PTSD is often complicated by comorbid anxiety and depression, substance misuse, uncontrollable anger and resulting violence, and interpersonal and vocational dysfunction. In the chronic phase of this illness, the intensity of PTSD symptoms fluctuates, mostly in response to social pressures and cues that remind patients of the trauma. Furthermore, a placebo effect, related to providing attention and support and following structured inquiry about the patient's condition, is likely to happen-even when no other specific treatment is provided.

> Treatment outcome measures should focus on those dimensions of PTSD that one wishes to change by providing treatment. These dimensions may range from a global assessment of personal, social, and vocational functioning to specific PTSD symptom domains, associated depression and anxiety, or more specific areas of functioning (e.g., avoidance or violence). The assessment of treatment effect on PTSD may also include criteria such as environmental stability and concurrent psychological stressors.

> Long-term studies and appropriate measures of the relevant dimensions of PTSD are needed to evaluate the sta

bility of the results beyond the shorter active phase of treatment studies.

REFERENCES

- 1. Shalev AY, Freedman S, Peri T, et al. Predicting PTSD in trauma survivors: prospective evaluation of self-report and clinician-administered instruments. Br J Psychiatry 1997;170:558-564
- 2. Shalev AY, Bonne O, Eth S. Treatment of posttraumatic stress disorder: a review. Psychosom Med 1996;58:165-182
- 3. Horowitz M, Wilner N, Alvarez W. Impact of Event Scale: a measure of subjective stress. Psychosom Med 1979;41:209-218
- 4. Davidson JR, Colket JT. The eight-item treatment-outcome post-traumatic stress disorder scale: a brief measure to assess treatment outcome in posttraumatic stress disorder. Int J Clin Psychopharmacol 1997;12:41-45
- 5. Shalev AY. Discussion: treatment of prolonged posttraumatic stress disorder: learning from experience [comment]. J Trauma Stress 1997;10: 415-423
- 6. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Washington, DC: American Psychiatric Association: 1994
- 7. LeDoux JE. Brain mechanisms of emotion and emotional learning. Curr Opin Neurobiol 1992;2:191–197
- 8. Lindemann E. Symptomatology and management of acute grief, 1944. Am J Psychiatry 1994;151(6, suppl):155–160
- 9. Macklin ML, Metzger LJ, Litz BT, et al. Lower precombat intelligence is a risk factor for posttraumatic stress disorder. J Consult Clin Psychol 1998; 66:323-326
- 10. Kessler RC, Sonnega A, Bromet E, et al. Posttraumatic stress disorder in the National Comorbidity Survey. Arch Gen Psychiatry 1995;52: 1048-1060
- 11. Shalev AY, Freedman S, Peri T, et al. Prospective study of posttraumatic stress disorder and depression following trauma. Am J Psychiatry 1998; 155:630-637
- 12. Freedman SA, Brandes D, Peri T, et al. Predictors of chronic post-traumatic stress disorder: a prospective study. Br J Psychiatry 1999;174:353-359
- 13. Johnson DR, Rosenheck R, Fontana A, et al. Outcome of intensive inpatient treatment for combat-related posttraumatic stress disorder. Am J Psychiatry 1996;153:771-777
- 14. Kolb LC. A neuropsychological hypothesis explaining posttraumatic stress disorders. Am J Psychiatry 1987;144:989-995
- 15. Shalev AY, Orr SP, Peri T, et al. Physiologic responses to loud tones in Israeli patients with posttraumatic stress disorder. Arch Gen Psychiatry 1992; 49:870-875
- 16. Hearst N, Newman TB, Hulley SB. Delayed effects of the military draft on mortality: a randomized natural experiment. N Engl J Med 1986;314: 620-624
- 17. Yehuda R, Schmeidler J, Siever LJ, et al. Individual differences in posttraumatic stress disorder symptom profiles in Holocaust survivors in concentration camps or in hiding. J Trauma Stress 1997;10:453-463
- 18. Scurfield RM, Kenderdine SK, Pollard RJ. Inpatient treatment for warrelated post-traumatic stress disorder: initial findings on a longer-term outcome study. J Trauma Stress 1990;3:185-201
- 19. van der Kolk BA, Dreyfuss D, Michaels M, et al. Fluoxetine in posttraumatic stress disorder. J Clin Psychiatry 1994;55:517-522
- 20. Stein MB, Walker JR, Hazen AL, et al. Full and partial posttraumatic stress disorder: findings from a community survey. Am J Psychiatry 1997;154: 1114-1119
- 21. Carlier IV, Gersons BP. Partial posttraumatic stress disorder (PTSD): the issue of psychological scars and the occurrence of PTSD symptoms. J Nerv Ment Dis 1995:183:107-109
- 22. Niles BL, Newman E, Fisher LM. Obstacles to assessment of PTSD in longitudinal research. In: Shalev AY, McFarlane AC, Yehuda R, eds. International Handbook of Human Response to Trauma. New York, NY: Plenum Press. In press
- 23. Forster PL, Schoenfeld FB, Marmar CR, et al. Lithium for irritability in post-traumatic stress disorder. J Trauma Stress 1995;8:143-149
- 24. Fesler FA. Valproate in combat-related posttraumatic stress disorder. J Clin Psychiatry 1991;52:361-364
- 25 Bleich A, Koslowsky M, Dolev A, et al. Post-traumatic stress disorder and depression: an analysis of comorbidity. Br J Psychiatry 1997;170:479-482
- 26. Hyer L, McCranie EW, Woods MG, et al. Suicidal behavior among chronic

Vietnam theatre veterans with PTSD. J Clin Psychol 1990;46:713-721

- 27. Hendin H, Haas AP. Suicide and guilt as manifestations of PTSD in Vietnam combat veterans. Am J Psychiatry 1991;148:586-591
- 28. Spitzer RL, Williams JBW, Gibbon M, et al. Structured Clinical Interview for DSM-IV (SCID-IV). New York, NY: Biometric Research, New York State Psychiatric Institute; 1994
- Blake DD, Weathers FW, Nagy LM, et al. A clinician rating scale for as-29 sessing current and lifetime PTSD: the CAPS-1. Behav Therapist 1990;13: 187-188
- 30. Blake DD, Weathers FW, Nagy LM, et al. The development of a clinicianadministered PTSD scale. J Trauma Stress 1995;8:75-90
- 31. Foa EB, Cashman L, Jaycox L, et al. The validation of a self-report measure of posttraumatic stress disorder, the Posttraumatic Diagnostic Scale. Psychol Assess 1997;9:445-451
- 32. Weiss DS, Marmar CR. The Impact of Event Scale, Revised. In: Wison JP, Keane TM, eds. Assessing Psychological Trauma and PTSD: A Practioner's Handbook. New York, NY: Guilford Press; 1997:399-411
- 33. Schwarzwald J, Solomon Z, Weisenberg M, et al. Validation of the Impact of Event Scale for psychological sequelae of combat. J Consult Clin Psychol 1987;55:251-256
- 34. Davidson JR, Book SW, Colket JT, et al. Assessment of a new self-rating scale for post-traumatic stress disorder. Psychol Med 1997;27:153-160
- 35. Keane TM, Caddell JM, Taylor KL. Mississippi Scale for Combat-Related Posttraumatic Stress Disorder: three studies in reliability and validity. J Consult Clin Psychol 1988;56:85-90
- 36. Vreven DL, Gudanowski DM, King LA, et al. The civilian version of the Mississippi PTSD Scale: a psychometric evaluation. J Trauma Stress 1995; 8:91-109
- 37. Davidson JRT, Smith RD, Kudler HS. Validity and reliability of the DSM-III criteria for posttraumatic stress disorder: experience with a structured interview (SI-PTSD). J Nerv Ment Dis 1989;177:336-341
- 38. Guy W. ECDEU Assessment Manual for Psychopharmacology. US Dept Health, Education, and Welfare publication (ADM) 76-338. Rockville, Md: National Institute of Mental Health; 1976:218-222
- 39 Bernstein EM, Putnam FW. Development, reliability, and validity of a dissociation scale. J Nerv Ment Dis 1986;174:727-735
- Beck AT, Ward CH, Mendelson M, et al. An inventory for measuring depression. Arch Gen Psychiatry 1961;4:561–571 41. Montgomery SA, Asberg M. A new depression rating scale designed to be
- sensitive to change. Br J Psychiatry 1979;134:382-389
- 42. Spielberger CD, Gorusch RL, Lushene RE. Manual for the State-Trait Anxiety Inventory. Palo Alto, Calif: Consulting Psychologists Press; 1970
- 43. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry 1960;23;56-62
- 44. Hamilton M. The assessment of anxiety states by rating. Br J Med Psychol 1959;32:50-55
- 45. Leon AC, Olfson M, Portera L, et al. Assessing psychiatric impairment in primary care with the Sheehan Disability Scale. Int J Psychiatry Med 1997;27:93-105
- 46. Connor KM, Sutherland SM, Tupler LA, et al. Fluoxetine in post-traumatic stress disorder. Br J Psychiatry 1999;175:17-22
- 47. Endicott J, Nee J, Harrison W, et al. Quality of life enjoyment and satisfaction questionnaire: a new measure. Psychopharmacol Bull 1993:29: 321-326
- 48. Brady K, Farfel G, and the Sertraline PTSD Study Group. Double-blind multicenter comparison of sertraline and placebo in PTSD. Paper presented at the 37th annual meeting of the American College of Neuropsychopharmacology; Dec 14-17, 1998; Los Croabas, Puerto Rico
- 49. Davidson J, Kudler H, Smith R, et al. Treatment of posttraumatic stress disorder with amitriptyline and placebo. Arch Gen Psychiatry 1990;47: 259-266
- 50. Kosten TR, Frank JB, Dan E, et al. Pharmacotherapy for posttraumatic stress disorder using phenelzine or imipramine. J Nerv Ment Dis 1991;179: 366-370
- 51. Baker DG, Diamond BI, Gillette G, et al. A double-blind, randomized, placebo-controlled multi-center study of brofaromine in the treatment of posttraumatic stress disorder. Psychopharmacology (Berl) 1995;122:386-389
- 52. Katz RJ, Lott MH, Arbus P, et al. Pharmacotherapy of post-traumatic stress disorder with a novel psychotropic. Anxiety 1995;1:169-174
- 53. Davidson JRT, Londborg PD, Pearlstein T, et al. Double blind comparison of sertraline and placebo in patients with posttraumatic stress disorder. Presented at the 36th annual meeting of the American College of Neuropsychopharmacology; Dec 8-12, 1997; Waikoloa, Hawaii