Complete Summary

GUIDELINE TITLE

Practice guideline for the treatment of patients with panic disorder.

BIBLIOGRAPHIC SOURCE(S)

American Psychiatric Association (APA). Practice guideline for the treatment of patients with panic disorder. 2nd ed. Washington (DC): American Psychiatric Association (APA); 2009 Jan. 90 p. [609 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: American Psychiatric Association (APA). Practice guideline for the treatment of patients with panic disorder. Washington (DC): American Psychiatric Press, Inc; 1998. 86 p.

Practice guideline for the treatment of patients with panic disorder. Work Group on Panic Disorder. American Psychiatric Association (APA). Am J Psychiatry 1998 May;155(5 Suppl):1-34.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory information has been released:

- December 16, 2008 - Antiepileptic drugs: The U.S. Food and Drug Administration (FDA) has completed its analysis of reports of suicidality (suicidal behavior or ideation [thoughts]) from placebo-controlled clinical trials of drugs used to treat epilepsy, psychiatric disorders, and other conditions. Based on the outcome of this review, FDA is requiring that all manufacturers of drugs in this class include a Warning in their labeling and develop a Medication Guide to be provided to patients prescribed these drugs to inform them of the risks of suicidal thoughts or actions. FDA expects that the increased risk of suicidality is shared by all antiepileptic drugs and anticipates that the class labeling change will be applied broadly.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Panic disorder

GUIDELINE CATEGORY

Counseling
Diagnosis
Evaluation
Management
Prevention
Risk Assessment
Treatment

CLINICAL SPECIALTY

Geriatrics
Neurology
Pediatrics
Psychiatry
Psychology

INTENDED USERS

Physicians
Psychologists/Non-physician Behavioral Health Clinicians

GUIDELINE OBJECTIVE(S)

To assist the psychiatrist in caring for patients with panic disorder

TARGET POPULATION

Children, adolescents, and adults with panic disorder according to the criteria in the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (DSM-IV)

INTERVENTIONS AND PRACTICES CONSIDERED

Psychiatric Management

1. Therapeutic alliances
2. Psychiatric assessment and diagnostic evaluation, including past and present psychiatric and general medical history; history of substance use; personal history (e.g., major life events); social, occupational, and family history; review of patient's medications; previous treatments; review of systems; mental status examination; physical examination; and appropriate diagnostic tests as indicated
3. Assessment of suicide risk and functional impairment
4. Goal setting
5. Monitoring
6. Patient/family education
7. Coordination of care
8. Treatment adherence
9. Addressing early signs of relapse
10. Formulation and implementation of a treatment plan

Psychosocial Interventions

1. Cognitive behavioral therapy, which may include psychoeducation, self-monitoring, countering anxious beliefs, exposure to fear cues, modification of anxiety-maintaining behaviors, and relapse prevention
2. Panic-focused psychodynamic psychotherapy
3. Eye movement desensitization and reprocessing (not been formally tested or has been proven ineffective)
4. Supportive psychotherapy (inferior to standard treatments)
5. Combined treatments: antidepressants and cognitive behavioral therapy
6. Group therapy
7. Marital and family therapy
8. Patient support groups

Pharmacologic Interventions

1. Selective serotonin reuptake inhibitors (SSRIs): citalopram, escitalopram, fluoxetine, sertraline, paroxetine, and fluvoxamine, paroxetine controlled release
2. Serotonin-norepinephrine reuptake inhibitors (SNRIs): duloxetine, venlafaxine extended release
3. Tricyclic antidepressants (TCAs): including imipramine, desipramine, nortriptyline, and clomipramine
4. Benzodiazepines: including alprazolam, clonazepam, and lorazepam
5. Monoamine oxidase inhibitors (MAOIs)
6. Other therapies (anticonvulsants, antipsychotic agents, antihypertensives, buspirone)

MAJOR OUTCOMES CONSIDERED

- Frequency and severity of panic episodes
- Proportion of patients achieving remission (usually defined as the absence of panic attacks within a specified period of time)

- Relapse rates among panic-free or symptom-free patients receiving treatment over the course of several years
- Morbidity associated with panic episodes
- Patient functioning
- Remission rates
- Quality of life
- Side effects of medications

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Relevant updates to the literature were identified through a MEDLINE literature search for articles published since the initial guideline edition, published in 1997. Thus, relevant literature was identified through a computerized search of MEDLINE, using PubMed, for the period from 1994 to 2005. Using the key words "panic" OR "panic attack" OR "panic attacks" OR "panic disorder" OR "anxiety attack" OR "anxiety attacks" OR "agoraphobia" OR "agoraphobic," a total of 5,088 citations limited to articles on humans were found. Using PsycInfo (EBSCOHost), the same search strategy yielded 5,444 references. Using Psychoanalytic Electronic Publishing (http://www.p-e-p.org), a search of the terms "panic disorder" OR "agoraphobia" yielded 132 references. Additional, less formal, literature searches were conducted by American Psychiatric Association (APA) staff and individual work group members, to include references through mid-2007. Practice guidelines for the treatment of patients with panic disorder that have been published by other organizations also were reviewed. The Cochrane databases were also searched for relevant meta-analyses. Sources of funding were considered when the work group reviewed the literature but are not always identified in this document.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Evidence tables were developed that reviewed the key features of each identified study, including funding source, study design, sample sizes, subject characteristics, treatment characteristics, and treatment outcomes.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

This practice guideline was developed under the auspices of the Steering Committee on Practice Guidelines. The development process is detailed in a document entitled "APA Guideline Development Process," which is available from the APA Department of Quality Improvement and Psychiatric Services or at www.psychiatryonline.com. Key features of this process include the following:

- A comprehensive literature review to identify all relevant randomized clinical trials as well as less rigorously designed clinical trials and case series when evidence from randomized trials was unavailable
- Development of evidence tables that reviewed the key features of each identified study, including funding source, study design, sample sizes, subject characteristics, treatment characteristics, and treatment outcomes
- Initial drafting of the guideline by a work group that included psychiatrists with clinical and research expertise in panic disorder
- Production of multiple revised drafts with widespread review; 29 organizations and 80 individuals submitted significant comments
- Approval by the APA Assembly and Board of Trustees
- Planned revisions at regular intervals

This document represents a synthesis of current scientific knowledge and rational clinical practice regarding the treatment of patients with panic disorder. It strives to be as free as possible of bias toward any theoretical approach to treatment. In order for the reader to appreciate the evidence base behind the guideline recommendations and the weight that should be given to each recommendation, the summary of treatment recommendations is keyed according to the level of confidence with which each recommendation is made. Each rating of clinical confidence considers the strength of the available evidence and is based on the best available data. When evidence is limited, the level of confidence also incorporates clinical consensus with regard to a particular clinical decision. In the listing of cited references, each reference is followed by a letter code in brackets that indicates the nature of the supporting evidence.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Each recommendation is identified as falling into one of three categories of endorsement, indicated by a bracketed Roman numeral following the statement. The three categories represent varying levels of clinical confidence:

[I] Recommended with substantial clinical confidence

[II] Recommended with moderate clinical confidence

[III] May be recommended on the basis of individual circumstances

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Iterative guideline drafts were reviewed by the Steering Committee, other experts, allied organizations, American Psychiatric Association (APA) members, and the APA Assembly and Board of Trustees; substantial revisions addressed or integrated the comments of these multiple reviewers.

This practice guideline was approved in July 2008 and published in January 2009.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The rating scheme for the strength of the recommendations (I, II, III) is repeated at the end of the "Major Recommendations" field.

Psychiatric Management

Panic disorder is a common and often disabling mental disorder. Treatment is indicated when symptoms of the disorder interfere with functioning or cause significant distress **[I]**. Effective treatment for panic disorder should lead not only to reduction in frequency and intensity of panic attacks, but also reductions in anticipatory anxiety and agoraphobic avoidance, optimally with full remission of symptoms and return to a premorbid level of functioning **[I]**. Psychiatric management consists of a comprehensive array of activities and interventions that should be instituted for all patients with panic disorder, in combination with specific modalities that have demonstrated efficacy **[I]**.

Establishing a Therapeutic Alliance

Psychiatrists should work to establish and maintain a therapeutic alliance so that the patient's care is a collaborative endeavor **[I]**. Careful attention to the patient's preferences and concerns with regard to treatment is essential to fostering a strong alliance **[I]**. In addition, education about panic disorder and its treatment should be provided in language that is readily understandable to the patient **[I]**. Many patients with panic disorder are fearful of certain aspects of treatment (e.g., medication side effects, confronting agoraphobic situations). A strong therapeutic alliance is important in supporting the patient through phases of treatment that may be anxiety provoking **[I]**.

Performing the Psychiatric Assessment

Patients should receive a thorough diagnostic evaluation both to establish the diagnosis of panic disorder and to identify other psychiatric or general medical conditions **[I]**. This evaluation generally includes a history of the present illness and current symptoms; past psychiatric history; general medical history; history of substance use; personal history (e.g., major life events); social, occupational, and family history; review of the patient's medications; previous treatments; review of systems; mental status examination; physical examination; and appropriate diagnostic tests (to rule out possible medical causes of panic symptoms) as indicated **[I]**. Assessment of substance use should include illicit drugs, prescribed and over-the-counter medications, and other substances (e.g., caffeine) that may produce physiological effects that can trigger or exacerbate panic symptoms **[I]**.

Delineating the specific features of panic disorder that characterize a given patient is an essential element of assessment and treatment planning **[I]**. It is crucial to determine if agoraphobia is present and to establish the extent of situational fear and avoidance **[I]**. The psychiatrist also should evaluate other psychiatric disorders, as co-occurring conditions may affect the course, treatment, and prognosis of panic disorder **[I]**. It must be determined that panic attacks do not occur solely as a result of a general medical condition or substance use and that they are not better conceptualized as a feature of another diagnosis **[I]**. The presence of medical disorders, substance use, and other psychiatric disorders does not preclude a concomitant diagnosis of panic disorder. If the symptoms of panic disorder are not deemed solely attributable to these factors, then diagnosing (and treating) both panic disorder and another condition may be warranted **[I]**.

Tailoring the Treatment Plan for the Individual Patient

Tailoring the treatment plan to match the needs of the particular patient requires a careful assessment of the frequency and nature of the patient's symptoms **[I]**. It may be helpful, in some circumstances, for patients to monitor their panic symptoms using techniques such as keeping a daily diary **[I]**. Such monitoring can aid in identification of triggers for panic symptoms, which may become a focus of subsequent intervention.

Continuing evaluation and management of co-occurring psychiatric and/or medical conditions is also essential to developing a treatment plan for an individual patient **[I]**. Co-occurring conditions may influence both selection and implementation of pharmacological and psychosocial treatments for panic disorder **[I]**.

Evaluating the Safety of the Patient

A careful assessment of suicide risk is necessary for all patients with panic disorder **[I]**. Panic disorder has been shown to be associated with an elevated risk of suicidal ideation and behavior, even in the absence of co-occurring conditions such as major depression. An assessment of suicidality includes identification of specific psychiatric symptoms known to be associated with suicide attempts or suicide; assessment of past suicidal behavior, family history of suicide and mental illness, current stressors, and potential protective factors such as positive reasons for living; and specific inquiry about suicidal thoughts, intent, plans, means, and behaviors **[I]**.

Evaluating Types and Severity of Functional Impairment

Panic disorder can impact numerous spheres of life including work, school, family, social relationships, and leisure activities. The psychiatrist should develop an understanding of how panic disorder affects the patient's functioning in these domains **[I]** with the aim of developing a treatment plan intended to minimize impairment **[I]**.

Establishing Goals for Treatment

All treatments for panic disorder aim to reduce the frequency and intensity of panic attacks, anticipatory anxiety, and agoraphobic avoidance, optimally with full remission of symptoms and return to a premorbid level of functioning **[I]**. Treatment of co-occurring psychiatric disorders when they are present is an additional goal **[I]**. The intermediate objectives that will help achieve these goals will depend on the chosen modality or modalities **[I]**.

Monitoring the Patient's Psychiatric Status

The different elements of panic disorder may resolve at different points during the course of treatment (e.g., panic attacks may remit before agoraphobic avoidance is eliminated). The psychiatrist should continue to monitor the status of all symptoms originally presented by the patient **[I]**. Psychiatrists may consider using rating scales to help monitor the patient's status at each session **[I]**. Patients also can be asked to keep a daily diary of panic symptoms to aid in ongoing assessment **[I]**.

Providing Education to the Patient and, When Appropriate, to the Family

Education alone may relieve some of the symptoms of panic disorder by helping the patient realize that his or her symptoms are neither life-threatening nor uncommon. Thus, once a diagnosis of panic disorder is made, the patient should be informed of the diagnosis and educated about panic disorder and treatment options **[I]**. Regardless of the treatment modality selected, it is important to inform the patient that in almost all cases the physical sensations that characterize panic attacks are not acutely dangerous and will abate **[I]**. Educational tools such as books, pamphlets, and trusted web sites can augment the face-to-face education provided by the psychiatrist **[I]**.

Providing the family with accurate information about panic disorder and its treatment is also important for many patients **[I]**. Education sometimes includes discussion of how changes in the patient's status affect the family system and of how responses of family members can help or hinder treatment of the patient's panic disorder **[II]**.

Patient education also includes general promotion of healthy behaviors such as exercise, good sleep hygiene, and decreased use of caffeine, tobacco, alcohol, and other potentially deleterious substances **[I]**.

Coordinating the Patient's Care with Other Clinicians

Many patients with panic disorder will be evaluated by or receive treatment from other health care professionals in addition to the psychiatrist. Under such circumstances, the clinicians should communicate periodically to ensure that care is coordinated and that treatments are working in synchrony **[I]**.

It is important to ensure that a general medical evaluation has been done (either by the psychiatrist or by another health care professional) to rule out medical causes of panic symptoms **[I]**. Extensive or specialized testing for medical causes of panic symptoms is usually not indicated but may be conducted based on individual characteristics of the patient **[III]**.

Enhancing Treatment Adherence

Problems with treatment adherence can result from a variety of factors (e.g., avoidance that is a manifestation of panic disorder, logistical barriers, cultural or language barriers, problems in the therapeutic relationship). Whenever possible, the psychiatrist should assess and acknowledge potential barriers to treatment adherence and should work collaboratively with the patient to minimize their influence **[I]**.

Many standard pharmacological and psychosocial treatments for panic disorder can be associated with short-term intensification of anxiety (e.g., because of medication side effects or exposure to fear cues during therapy). These temporary increases in anxiety may contribute to decreased treatment adherence. The psychiatrist should adopt a stance that encourages patients to articulate their fears about treatment and should provide patients with a realistic notion of what they can expect at different points in treatment **[I]**. In particular, patients should be informed about when a positive response to treatment can be expected so that they do not prematurely abandon treatment due to misconceptions about the time frame for response **[I]**. Patients should also be encouraged to contact the psychiatrist (e.g., by telephone if between visits) if they have concerns or questions, as these can often be readily addressed and lead to enhanced treatment adherence **[I]**.

Working with the Patient to Address Early Signs of Relapse

Although standard treatments effectively reduce the burden of panic disorder for the majority of patients, even some patients with a good treatment response may continue to have lingering symptoms (e.g., occasional panic attacks) or have a

recurrence of symptoms after remission. Patients should be reassured that fluctuations in symptoms can occur during the course of treatment before an acceptable level of remission is reached **[I]**. Patients should also be informed that symptoms of panic disorder may recur even after remission and be provided with a plan for how to respond **[I]**.

Formulation and Implementation of a Treatment Plan

Choosing a Treatment Setting

The treatment of panic disorder is generally conducted entirely on an outpatient basis, as the condition by itself rarely warrants hospitalization **[I]**. However, it may be necessary to hospitalize a patient with panic disorder because of symptoms of co-occurring disorders (e.g., when acute suicidality associated with a mood disorder is present or when inpatient detoxification is required for a substance use disorder) **[I]**. Under such circumstances, the treatment of panic disorder can be initiated in the hospital along with treatment of the disorder that prompted hospitalization **[I]**. Rarely, hospitalization or partial hospitalization is required in very severe cases of panic disorder with agoraphobia when administration of outpatient treatment has been ineffective or is impractical **[I]**. Home visits are another treatment option for patients with severe agoraphobia who are limited in their ability to travel or leave the house **[II]**. When accessibility to mental health care is limited (e.g., in remote or underserved areas), telephone- or Internet-based treatments may be considered **[II]**.

Choosing an Initial Treatment Modality

A range of specific psychosocial and pharmacological interventions have proven benefits in treating panic disorder. The use of a selective serotonin reuptake inhibitor (SSRI), serotonin-norepinephrine reuptake inhibitor (SNRI), tricyclic antidepressant (TCA), benzodiazepine (appropriate as monotherapy only in the absence of a co-occurring mood disorder), or cognitive-behavioral therapy (CBT) as the initial treatment for panic disorder is strongly supported by demonstrated efficacy in numerous randomized controlled trials **[I]**. A particular form of psychodynamic psychotherapy, panic-focused psychodynamic psychotherapy (PFPP), was effective in one randomized controlled trial and could be offered as an initial treatment under certain circumstances **[II]**.

There is insufficient evidence to recommend any of these pharmacological or psychosocial interventions as superior to the others, or to routinely recommend a combination of treatments over monotherapy **[II]**. Although combination treatment does not appear to be significantly superior to standard monotherapy as initial treatment for most individuals with panic disorder, psychiatrists and patients may choose this option based on individual circumstances (e.g., patient preference) **[II]**.

Considerations that guide the choice of an initial treatment modality include patient preference, the risks and benefits for the particular patient, the patient's past treatment history, the presence of co-occurring general medical and other psychiatric conditions, cost, and treatment availability **[I]**. Psychosocial treatment (with the strongest evidence available for CBT) is recommended for patients who prefer nonmedication treatment and can invest the time and effort required to

attend weekly sessions and complete between-session practices **[I]**. One caveat is that CBT and other specialized psychosocial treatments are not readily available in some geographic areas. Pharmacotherapy (usually with an SSRI or serotonin-norepinephrine reuptake inhibitor [SNRI]) is recommended for patients who prefer this modality or who do not have sufficient time or other resources to engage in psychosocial treatment **[I]**. Combined treatment should be considered for patients who have failed to respond to standard monotherapies and may also be used under certain clinical circumstances (e.g., using pharmacotherapy for temporary control of severe symptoms that are impeding the patient's ability to engage in psychosocial treatment) **[II]**. Adding psychosocial treatment to pharmacotherapy either from the start, or at some later point in treatment, may enhance long-term outcomes by reducing the likelihood of relapse when pharmacological treatment is stopped **[II]**.

Evaluating Whether the Treatment Is Working

After treatment is initiated, it is important to monitor change in key symptoms such as frequency and intensity of panic attacks, level of anticipatory anxiety, degree of agoraphobic avoidance, and severity of interference and distress related to panic disorder **[I]**. Effective treatment should produce a decrease in each of these domains, although some may change more quickly than others. The severity of co-occurring conditions also should be assessed at regular intervals, as treatment of panic disorder can influence co-occurring conditions (e.g., major depression; other anxiety disorders) **[I]**. Rating scales are a useful adjunct to ongoing clinical assessment for the purpose of evaluating treatment outcome **[I]**.

Determining If and When to Change Treatment

Some individuals do not respond, or respond incompletely, to first-line treatments for panic disorder. Whenever treatment response is unsatisfactory, the psychiatrist should first consider the possible contribution of fundamental clinical factors such as an underlying untreated medical illness that accounts for the symptoms, interference by co-occurring general medical or psychiatric conditions (including depression and substance use), inadequate treatment adherence, problems in the therapeutic alliance, the presence of psychosocial stressors, motivational factors, and inability to tolerate a particular treatment **[I]**. These potential impediments to successful treatment should be addressed as early as possible in treatment **[I]**. In addition, if panic-related concerns are leading the patient to minimize the impact of avoidance or accept functional limitations, the patient should be encouraged to think through the costs and benefits of accepting versus treating functional limitations **[I]**. Clinicians should be reluctant to accept partial improvement as a satisfactory outcome and should aim for remission whenever feasible **[I]**.

If response to treatment remains unsatisfactory, and if an adequate trial has been attempted, it is appropriate for the psychiatrist and the patient to consider a change **[I]**. Decisions about whether and how to make changes will depend on the level of response to the initial treatment (i.e., none versus partial), the palatability and feasibility of other treatment options for a given patient, and the level of symptoms and impairment that remain **[I]**. Persistent significant symptoms of panic disorder despite a lengthy course of a particular treatment

should trigger a reassessment of the treatment plan, including possible consultation with another qualified professional **[I]**.

Approaches to Try When a First-Line Treatment Is Unsuccessful

If fundamental clinical issues have been addressed and it is determined that a change is desirable, the psychiatrist and patient can either augment the current treatment by adding another agent (in the case of pharmacotherapy) or another modality (i.e., add CBT if the patient is already receiving pharmacotherapy, or add pharmacotherapy if the patient is already receiving CBT) **[I]**, or they can decide to switch to a different medication or therapeutic modality **[I]**. Decisions about how to address treatment resistance are usually highly individualized and based on clinical judgment, since few studies have tested the effects of specific switching or augmentation strategies. However, augmentation is generally a reasonable approach if some significant benefits were observed with the original treatment **[II]**. On the other hand, if the original treatment failed to provide any significant alleviation of the patient's symptoms, a switch in treatment may be more useful **[II]**.

If one first-line treatment (e.g., CBT, an SSRI, an SNRI) has failed, adding or switching to another first-line treatment is recommended **[I]**. Adding a benzodiazepine to an antidepressant is a common augmentation strategy to target residual symptoms **[II]**. If the treatment options with the most robust evidence have been unsuccessful, other options with some empirical support can be considered (e.g., a monoamine oxidase inhibitor [MAOI], panic-focused psychodynamic psychotherapy) **[II]**. After first- and second-line treatments and augmentation strategies have been exhausted (either due to lack of efficacy or intolerance of the treatment by the patient), less well-supported treatment strategies may be considered **[III]**. These include monotherapy or augmentation with gabapentin or a second-generation antipsychotic or with a psychotherapeutic intervention other than CBT or panic-focused psychodynamic psychotherapy **[III]**. Psychiatrists are encouraged to seek consultation from experienced colleagues when developing treatment plans for patients whose symptoms have been resistant to standard treatments for panic disorder **[I]**.

Specific Psychosocial Interventions

Psychosocial treatments for panic disorder should be conducted by professionals with an appropriate level of training and experience in the relevant approach **[I]**. Based on the current available evidence, CBT is the psychosocial treatment that would be indicated most often for patients presenting with panic disorder **[I]**. Cognitive-behavioral therapy is a time-limited treatment (generally 10–15 weekly sessions) with durable effects. It can be successfully administered individually or in a group format **[I]**. Self-directed forms of CBT may be useful for patients who do not have ready access to a trained CBT therapist **[II]**. Cognitive-behavioral therapy for panic disorder generally includes psychoeducation, self-monitoring, countering anxious beliefs, exposure to fear cues, modification of anxiety-maintaining behaviors, and relapse prevention **[I]**. Exposure therapy, which focuses almost exclusively on systematic exposure to fear cues, is also effective **[I]**.

Panic-focused psychodynamic psychotherapy also has demonstrated efficacy for panic disorder, although its evidence base is more limited. Panic-focused psychodynamic psychotherapy may be indicated as an initial psychosocial treatment in some cases (e.g., patient preference) **[II]**. Panic-focused psychodynamic psychotherapy is a time-limited treatment (twice weekly for 12 weeks) that is administered on an individual basis. Panic-focused psychodynamic psychotherapy utilizes the general principles of psychodynamic psychotherapy, with special focus on the transference as the therapeutic agent promoting change, and encourages patients to confront the emotional significance of their panic symptoms with the aim of promoting greater autonomy, symptom relief, and improved functioning. Although psychodynamic psychotherapies (other than panic-focused psychodynamic psychotherapy) that focus more broadly on emotional and interpersonal issues have not been formally tested for panic disorder, some case report data and clinical experience suggest this approach may be useful for some patients **[III]**.

Other psychosocial treatments have not been formally tested for panic disorder or have proven ineffective (e.g., eye movement desensitization and reprocessing [EMDR]) or inferior to standard treatments such as CBT (e.g., supportive psychotherapy).

Group CBT is effective and can be recommended for treatment of panic disorder **[I]**. Other group therapies (including patient support groups) are not recommended as monotherapies for panic disorder, although they may be useful adjuncts to other effective treatments for some patients **[III]**.

Couples or family therapy alone is not recommended as a treatment for panic disorder, although it may be helpful in addressing co-occurring relationship dysfunction **[III]**. It can be beneficial to include significant others in CBT (e.g., partner-assisted exposure therapy for agoraphobia), especially if they are educated in the cognitive-behavioral model of panic disorder and enlisted to help with between-session practices **[II]**. When pursuing other treatments for panic disorder (e.g., pharmacotherapy), education of significant others about the nature of the disorder and enlisting significant others to improve treatment adherence may also be helpful **[III]**.

Specific Pharmacological Interventions

Selective serotonin reuptake inhibitors, SNRIs, tricyclic antidepressants (TCAs), and benzodiazepines have demonstrated efficacy in numerous controlled trials and are recommended for treatment of panic disorder **[I]**. Monoamine oxidase inhibitors appear effective for panic disorder but, because of their safety profile, they are generally reserved for patients who have failed to respond to several first-line treatments **[II]**. Other medications with less empirical support (e.g., mirtazapine, anticonvulsants such as gabapentin) may be considered as monotherapies or adjunctive treatments for panic disorder when patients have failed to respond to several standard treatments or based on other individual circumstances **[III]**.

Because SSRIs, SNRIs, TCAs, and benzodiazepines appear roughly comparable in their efficacy for panic disorder, selecting a medication for a particular patient mainly involves considerations of side effects (including any applicable warnings

from the U.S. Food and Drug Administration [FDA]), cost, pharmacological properties, potential drug interactions, prior treatment history, co-occurring general medical and psychiatric conditions, and the strength of the evidence base for the particular medication in treatment of panic disorder **[I]**. The relatively favorable safety and side effect profile of SSRIs and SNRIs makes them the best initial choice for many patients with panic disorder **[I]**. Although TCAs are effective, the side effects and greater toxicity in overdose associated with them often limit their acceptability to patients and their clinical utility. Selective serotonin reuptake inhibitors, SNRIs, and TCAs are all preferable to benzodiazepines as monotherapies for patients with co-occurring depression or substance use disorders **[I]**. Benzodiazepines may be especially useful adjunctively with antidepressants to treat residual anxiety symptoms **[II]**. Benzodiazepines may be preferred (as monotherapies or in combination with antidepressants) for patients with very distressing or impairing symptoms in whom rapid symptom control is critical **[II]**. The benefit of more rapid response to benzodiazepines must be balanced against the possibilities of troublesome side effects (e.g., sedation) and physiological dependence that may lead to difficulty discontinuing the medication **[I]**.

Patients should be educated about the likely time course of treatment effects associated with a particular medication **[I]**. Because patients with panic disorder can be sensitive to medication side effects, low starting doses of SSRIs, SNRIs, and TCAs (approximately half of the starting doses given to depressed patients) are recommended **[I]**. The low dose is maintained for several days then gradually increased to a full therapeutic dose over subsequent days and as tolerated by the patient **[I]**. Underdosing of antidepressants (i.e., starting low and then not increasing gradually to full therapeutic dosages as needed) is common in treatment of panic disorder and is a frequent source of partial response or nonresponse **[II]**. A regular dosing schedule rather than a p.r.n. ("as needed") schedule is preferred for patients with panic disorder who are taking benzodiazepines **[II]**, where the goal is to prevent panic attacks rather than reduce symptoms once an attack has already occurred.

Once an initial pharmacotherapy has been selected, patients are typically seen every 1–2 weeks when first starting a new medication, then every 2–4 weeks until the dose is stabilized **[I]**. After the dose is stabilized and symptoms have decreased, patients will most likely require less frequent visits **[I]**.

When considering any specific medication, the psychiatrist must balance the risks associated with the medication against the clinical need for pharmacotherapy **[I]**. The Food and Drug Administration has warned of the possibility that antidepressants may increase the risk of suicidal ideation and behavior in patients age 25 years and younger; this is an important factor to consider before using an SSRI, an SNRI, or a TCA for panic disorder. Other important safety considerations for SSRIs include possible increased likelihood of upper gastrointestinal bleeding (particularly when taken in combination with non-steroidal anti-inflammatory drugs [NSAIDs] or with aspirin) and increased risk of falls and osteoporotic fractures in patients age 50 years and older. With venlafaxine extended release (ER), a small proportion of patients may develop sustained hypertension. It is recommended that psychiatrists assess blood pressure during treatment, particularly when venlafaxine extended release is titrated to higher doses **[I]**.

Tricyclic antidepressants should not be prescribed for patients with panic disorder who also have acute narrow-angle glaucoma or clinically significant prostatic hypertrophy. Tricyclic antidepressants may increase the likelihood of falls, particularly among elderly patients. A baseline electrocardiogram should be considered before initiating a TCA, because patients with preexisting cardiac conduction abnormalities may experience significant or fatal arrhythmia with TCA treatment. Overdoses with TCAs can lead to significant cardiac toxicity and fatality, and therefore TCAs should be used judiciously in suicidal patients.

Benzodiazepines may produce sedation, fatigue, ataxia, slurred speech, memory impairment, and weakness. Geriatric patients taking benzodiazepines may be at higher risk for falls and fractures. Because of an increased risk of motor vehicle accidents with benzodiazepine use, patients should be warned about driving or operating heavy machinery while taking benzodiazepines **[I]**. Patients should also be advised about the additive effects of benzodiazepines and alcohol **[I]**. Caution and careful monitoring is indicated when prescribing benzodiazepines to elderly patients, those with preexisting cognitive impairment, or those with a history of substance use disorder **[I]**.

For women with panic disorder who are pregnant, nursing, or planning to become pregnant, psychosocial interventions should be considered in lieu of pharmacotherapy **[II]**. Pharmacotherapy may also be indicated **[III]** but requires weighing and discussion of the potential benefits and risks with the patient, her obstetrician, and, whenever possible, her partner **[I]**. Such discussions should also consider the potential risks to the patient and the child of untreated psychiatric illness, including panic disorder and any co-occurring psychiatric conditions **[I]**.

Maintaining or Discontinuing Treatment After Response

Pharmacotherapy should generally be continued for 1 year or more after acute response to promote further symptom reduction and decrease risk of recurrence **[I]**. Incorporating maintenance treatment (e.g., monthly "booster" sessions focused on relapse prevention) into psychosocial treatments for panic disorder also may help maintain positive response **[II]**, although more systematic investigation of this issue is needed.

Before advising a taper of effective pharmacotherapy, the psychiatrist should consider several factors, including the duration of the patient's symptom stability, the presence of current or impending psychosocial stressors in the patient's life, and the extent to which the patient is motivated to discontinue the medication **[II]**. Discussion of medication taper should also include the possible outcomes of taper, which could include discontinuation symptoms and recurrence of panic symptoms **[I]**. If medication is tapered, it should be done in a collaborative manner with continual assessment of the effects of the taper and the patient's responses to any changes that emerge **[I]**.

If a decision is made to discontinue successful treatment with an SSRI, an SNRI, or a TCA, the medication should be gradually tapered (e.g., one dosage step down every month or two), thereby providing the opportunity to watch for recurrence and, if desired, to reinitiate treatment at a previously effective dose **[II]**. However, under more urgent conditions (e.g., the patient is pregnant and the

decision is made to discontinue medications immediately), these medications can be discontinued much more quickly **[I]**.

The approach to benzodiazepine discontinuation also involves a slow and gradual tapering of dose **[I]**. Withdrawal symptoms and symptomatic rebound are commonly seen with benzodiazepine discontinuation, can occur throughout the taper, and may be especially severe toward the end of the taper. This argues for tapering benzodiazepines very slowly for patients with panic disorder, probably over 2–4 months and at rates no higher than 10% of the dose per week **[I]**. Cognitive-behavioral therapy may be added to facilitate withdrawal from benzodiazepines **[I]**.

Definitions:

Grading of Recommendations

[I] Recommended with substantial clinical confidence

[II] Recommended with moderate clinical confidence

[III] May be recommended on the basis of individual circumstances

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The following coding system is used to indicate the nature of the supporting evidence in the summary recommendations and references:

[A] *Randomized clinical trial*. A study of an intervention in which subjects are prospectively followed over time; there are treatment and control groups; subjects are randomly assigned to the two groups; both the subjects and the investigators are blind to the assignments.

[A-] *Same as above*, but not double-blind

[B] *Clinical trial*. A prospective study in which an intervention is made and the results of that intervention are tracked longitudinally; study does not meet standards for a randomized clinical trial.

[C] *Cohort or longitudinal study*. A study in which subjects are prospectively followed over time without any specific intervention.

[D] *Case-control study*. A study in which a group of patients is identified in the present and information about them is pursued retrospectively or backward in time.

[E] *Review with secondary data analysis*. A structured analytic review of existing data, e.g., a meta-analysis or a decision analysis.

[F] *Review*. A qualitative review and discussion of previously published literature without a quantitative synthesis of the data.

[G] *Other*. Textbooks, expert opinions, case reports, and other reports not included above.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Effective treatment for panic disorder should lead to:
    - Reduction in frequency and intensity of panic attacks
    - Reductions in anticipatory anxiety and agoraphobic avoidance
    - Full remission of symptoms and return to premorbid level of functioning
- Medications may stop or reduce the frequency of panic attacks, as well as affect anticipatory anxiety, agoraphobic avoidance, limited symptom attacks, associated depression, and global function.
- Medication support groups may provide useful adjunctive experiences for patients.
- Patient support groups allow patients to learn that they are not unique in experiencing panic attacks and to share ways of coping with the illness. Family members of patients with panic disorder also may benefit from the educational aspects of patient support groups.

POTENTIAL HARMS

- Fears of physical exertion are common in patients with panic disorder and that exercise may actually trigger panic attacks in some patients (although most patients can tolerate exercise without difficulty).
- The exploration of memories and important conflicted relationships and the surfacing of unconscious material may sometimes be associated with powerful affects and transient upsets in the therapeutic and other relationships.
- Side effects from pharmacotherapy agents (see the original guideline document). In addition, the Food and Drug Administration (FDA) has warned of the possibility that selective serotonin reuptake inhibitors (SSRIs) and other antidepressants may increase the risk of suicidal ideation and behavior in patients age 25 years and younger.

Abrupt discontinuation of some pharmacotherapy agents can result in variety of neurological problems. See the original guideline document for more details.

Elderly Patients

The risk of falls may be increased by tricyclic antidepressants (TCAs), particularly among elderly patients, because of orthostasis.

Patients with Preexisting Cardiac Conduction Abnormalities

These patients may experience significant or fatal arrhythmia with TCA treatment, a baseline electrocardiogram should be considered before initiating a TCA.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Tricyclic antidepressants should not be prescribed for patients with panic disorder who also have acute narrow angle glaucoma or clinically significant prostatic hypertrophy.
- Certain medications, including but not limited to sympathomimetic amines and decongestants, can also precipitate a hypertensive crisis and must not be used with monoamine oxidase inhibitors (MAOIs).

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This guideline is not intended to be construed or to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual patient and are subject to change as scientific knowledge and technology advance and patterns evolve. These parameters of practice should be considered guidelines only. Adherence to them will not ensure a successful outcome for every individual, nor should they be interpreted as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgment regarding a particular clinical procedure or treatment plan must be made by the psychiatrist in light of the clinical data presented by the patient and the diagnostic and treatment options available.
- Medications discussed in this practice guideline may not have an indication from the U.S. Food and Drug Administration for the disorder or condition for which they are recommended. Off-label use of medications by individual physicians is permitted and common. Decisions about off-label use can be guided by the evidence provided in the American Psychiatric Association practice guideline, other scientific literature, and clinical experience.
- The American Psychiatric Association does not endorse the accuracy of the information contained in any of the publications or web sites listed in the Appendix in the original guideline document at the time of writing or in the future, although they are believed to be generally trustworthy at the time of writing. The psychiatrist should review a particular book or visit the particular web site before recommending it to a patient.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Quick Reference Guides/Physician Guides

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

American Psychiatric Association (APA). Practice guideline for the treatment of patients with panic disorder. 2nd ed. Washington (DC): American Psychiatric Association (APA); 2009 Jan. 90 p. [609 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1998 May (revised 2009 Jan)

GUIDELINE DEVELOPER(S)

American Psychiatric Association - Medical Specialty Society

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American Psychiatric Association (APA)

GUIDELINE COMMITTEE

Work Group on Panic Disorders

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

This practice guideline has been developed by psychiatrists who are in active clinical practice. In addition, some contributors are primarily involved in research or other academic endeavors. It is possible that through such activities some contributors, including work group members and reviewers, have received income related to treatments discussed in this guideline. A number of mechanisms are in place to minimize the potential for producing biased recommendations because of conflicts of interest. Work group members are selected on the basis of their expertise and integrity. Any work group member or reviewer who has a potential conflict of interest that may bias (or appear to bias) his or her work is asked to disclose this to the Steering Committee on Practice Guidelines and the work group.

- For the period from September 2005 to June 2008, Dr. Stein reports receiving research grants from the National Institute of Mental Health, the Department of Veterans Affairs, the Department of Defense, Eli Lilly and Company, Forest Pharmaceuticals, Inc., Hoffmann-La Roche, Inc., Novartis, Pfizer, GlaxoSmithKline, Solvay, UCB, and Wyeth. He reports receiving consultant fees from Allergan, Inc., ALZA Corporation, Alexza Molecular Delivery Corp., AstraZeneca, Avera Pharmaceuticals, BrainCells Inc., Bristol-Myers Squibb, Cephalon, Comprehensive NeuroScience, Eli Lilly and Company, EPI-Q Inc., Forest Pharmaceuticals, Inc., GlaxoSmithKline, Hoffmann-La Roche, Inc., Integral Health Decisions Inc., Janssen Research Foundation, Jazz Pharmaceuticals, Inc., Johnson & Johnson, Mindsite, Pfizer, sanofi-aventis, Solvay, Transcept Pharmaceuticals, Inc., UCB, and Wyeth. He reports receiving honoraria from Eli Lilly and Company, GlaxoSmithKline, Solvay, and Wyeth.
- For the period from October 2005 to June 2008, Dr. Goin reports no competing interests.
- For the period from September 2005 to June 2008, Dr. Pollack reports serving on advisory boards and doing consultation for AstraZeneca, BrainCells Inc., Bristol-Myers Squibb, Cephalon, Dov Pharmaceutical Inc., Forest Pharmaceuticals, Inc., GlaxoSmithKline, Janssen, Jazz Pharmaceuticals, Inc., Eli Lilly and Company, MedAvante, Neurocrine Biosciences, Neurogen Corp.,

Novartis, Otsuka Pharmaceutical, Pfizer, Predix Pharmaceuticals, Roche, sanofi-aventis, Sepracor Inc., Solvay, Tikvah Therapeutics, Inc., Transcept Pharmaceuticals, Inc., UCB, and Wyeth. He reports receiving research grants from AstraZeneca, Bristol-Myers Squibb, Cephalon, Cyberonics, Forest Pharmaceuticals, Inc., GlaxoSmithKline, Janssen, Eli Lilly and Company, National Alliance for Research on Schizophrenia and Depression, the National Institute on Drug Abuse, the National Institute of Mental Health, Pfizer, Roche, Sepracor Inc., UCB, and Wyeth. He reports receiving speaker fees from Bristol-Myers Squibb, Forest Pharmaceuticals, Inc., GlaxoSmithKline, Janssen, Eli Lilly and Company, Pfizer, Solvay, and Wyeth. He reports equity holdings in MedAvante and Mensante Corporation. He reports receiving copyright royalties for the Structured Interview Guide to the Hamilton-A (SIGH-A) and SAFER.

- For the period from August 2004 to June 2008, Dr. Roy-Byrne reports receiving consultant or advisory fees from Jazz Pharmaceuticals, Inc., and Solvay. He reports receiving speaker honoraria (via a continuing medical education company) from Forest Pharmaceuticals, Inc., Pfizer, and Wyeth.
- For the period from August 2005 to June 2008, Dr. Sareen reports receiving honoraria from Wyeth, AstraZeneca, Lundbeck, and GlaxoSmithKline.
- For the period from September 2005 to June 2008, Dr. Simon reports receiving research support from Cephalon, Pfizer, AstraZeneca, Forest Pharmaceuticals, Inc., GlaxoSmithKline, UCB, Sepracor Inc., Janssen Research Foundation, Eli Lilly and Company, National Alliance for Research on Schizophrenia and Depression, and the National Institute of Mental Health. She reports receiving consultant fees or honoraria from Paramount BioSciences, Anxiety Disorders Association of America, American Psychiatric Association, American Foundation for Suicide Prevention, Forest Pharmaceuticals, Inc., Solvay, Sepracor Inc., UCB, and Pfizer.
- For the period from November 2005 to June 2008, Dr. Campbell-Sills reports no competing interests.

The Executive Committee on Practice Guidelines has reviewed this guideline and found no evidence of influence from these relationships.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: American Psychiatric Association (APA). Practice guideline for the treatment of patients with panic disorder. Washington (DC): American Psychiatric Press, Inc; 1998. 86 p.

Practice guideline for the treatment of patients with panic disorder. Work Group on Panic Disorder. American Psychiatric Association (APA). Am J Psychiatry 1998 May;155(5 Suppl):1-34.

GUIDELINE AVAILABILITY

Electronic copies: Available from the American Psychiatric Association (APA) Web site.

Print copies: Available from the American Psychiatric Press, Inc (APPI), 1000 Wilson Boulevard, Suite 1825, Arlington, VA 22209-3901; (703) 907-7322; (800) 368-5777; fax (703) 907-1091.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Treating panic disorder. A quick reference guide. Washington (DC): American Psychiatric Association (APA); 2009 Jan. 23 p. Electronic copies: Available from the American Psychiatric Association (APA) Web site.

Print copies: Available from the American Psychiatric Press, Inc (APPI), 1000 Wilson Boulevard, Suite 1825, Arlington, VA 22209-3901; (703) 907-7322; (800) 368-5777; fax (703) 907-1091.

PATIENT RESOURCES

None available

NGC STATUS

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