

Identifying and Treating Panic Disorder in Primary Care

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Many individuals who experience a panic attack at some point in their lives will meet criteria for panic disorder. However, although most primary care physicians recognize broad-spectrum mood and anxiety disorders, they may not make a specific diagnosis such as major depressive disorder or panic disorder. Comorbid panic disorder and other anxiety conditions are a well-established phenomenon in depressive disorders and can have a negative impact on treatment and worsen prognosis. This negative impact underscores the importance of specifically identifying these disorders and their comorbidities. Although an analysis of other potential causes of presenting symptoms is at times indicated, diagnosis should be made positively by identifying the symptoms diagnostic of the anxiety conditions rather than negatively by eliminating other conditions. Treatment of patients with panic disorder can improve quality of life and productivity as well as reduce health care costs. Pharmacotherapy, cognitive-behavioral therapy, and collaborative relationships with patients and psychiatrists can all aid primary care physicians in providing acute and long-term treatment for patients with panic as well as other mood and anxiety disorders.

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Annually, 7.3% of adults experience a panic attack and 3% to 4% develop panic disorder.¹ Unfortunately, many patients with mood and anxiety disorders are evaluated by numerous physicians before a specific mental disorder is finally recognized and treatment initiated.¹ Although most primary care physicians recognize broad-spectrum mood and anxiety disorders, many do not make a distinct diagnosis such as major depressive disorder (MDD) or panic disorder. In the Primary Care Anxiety Project (PCAP), a long-term naturalistic study² of anxiety disorders among patients in primary care settings, we found that of 539 patients later identified as having had a specific mood or anxiety disorder according to DSM-IV criteria, 58% were diagnosed by a primary care physician with an unspecified mood or anxiety disorder and 16% as having no mood or anxiety disorder at all. Only 26% of the diagnoses made by primary care physicians matched the precise diagnoses subsequently made by a psychiatric specialist.

Üstün and Sartorius³ estimated that half of all patients with major depression also have an anxiety disorder. Using the primary care version of the Composite International Diagnostic Interview and prevalence data from primary health clinics in 15 countries, they found that 62% of patients with a depressive disorder suffered from at least

one other current mental disorder, and the most frequent were anxiety disorders. Comorbid panic disorder is a well-established phenomenon in depressive disorders that can complicate treatment and significantly worsen long-term prognosis. Patients with comorbid panic and depression have been found to have longer and more severe depressive episodes,⁴ to miss work 4 times more often,⁵ and to attempt suicide more frequently than patients with either disorder alone.⁵ The PCAP study⁶ showed that while 16% to 18% of patients with panic disorder alone reported past suicide attempts, 25% to 32% of those with panic disorder and major depression had a lifetime history of suicide attempts.

The negative impact that coexisting panic disorder can have on prognosis and treatment of depression underscores the importance of specifically identifying anxiety disorders in primary care. Panic disorder by itself is associated with pervasive social and health consequences similar to those of major depression (e.g., increased use of the emergency department, financial dependency, and marital discord).⁷ Markowitz et al.⁷ reported decreases in nonpsychiatric medical visits, hospitalizations, laboratory tests, and lost productivity among patients with panic disorder treated for 1 year.

IDENTIFYING PANIC DISORDER

The recognition of panic attacks and panic disorder in primary care depends on a positive identification of symptoms and impact on functioning rather than eliminating other conditions. Unlike most patients with depression or other anxiety disorders, patients with panic disorder often have very specific and dramatic cardiac and nervous system symptoms that are worrisome to patients as well as to primary care physicians. While many medical conditions mimic panic disorder, the majority of panic attacks seen in

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Table 1. Diagnostic Criteria for Panic Attack, Panic Disorder, and Panic Disorder With Agoraphobia^a**Diagnostic Criteria for Panic Attack**

A discrete period of intense fear or discomfort in which 4 or more of the following symptoms developed abruptly and reached a peak within 10 minutes:

- Cardiovascular
 - Chest pain or discomfort
 - Shortness of breath or smothering
 - Palpitations, pounding heart, or accelerated heart rate
- Neurologic
 - Trembling or shaking
 - Paresthesias (numbness or tingling)
 - Feeling dizzy, unsteady, light-headed or faint
- Autonomic
 - Sweating
 - Chills or hot flushes
- Gastrointestinal
 - Choking feeling
 - Nausea or abdominal distress
- Psychiatric
 - Derealization (feelings of unreality) or depersonalization (being detached from oneself)
 - Fear of losing control or going crazy
 - Fear of dying

Diagnostic Criteria for Panic Disorder

Recurrent unexpected panic attacks

At least 1 of the attacks has been followed by 1 or more of the following for at least 1 month:

- Persistent concern about having additional attacks
- Worry about the implications of the attack or its consequences
- A significant change in behavior related to the attacks

Panic attacks not due to physiologic effects of a substance or medical condition

Panic attacks not better accounted for by another mental disorder

Diagnostic Criteria for Panic Disorder With Agoraphobia

Panic disorder accompanied by agoraphobia, or anxiety about being in situations in which escape might be difficult (or embarrassing) or in which help might not be available in the event of having a panic attack

^aBased on the American Psychiatric Association DSM-IV.

primary care are psychogenic in origin, and those that are not are relatively easy to differentiate from an episode of panic. Key symptoms of a panic attack are intense fear of losing control, fear of dying, and feelings of unreality. These symptoms usually do not accompany or may be less prominent than key symptoms associated with medical conditions. Some conditions that may appear as panic disorder include mitral valve prolapse, hyperthyroidism, hypothyroidism, diabetes mellitus, hypoglycemia, migraine headaches, temporal lobe seizure, vestibular dysfunction, myocardial infarction, hypertension, hypotension, asthma, and transient ischemia.

Somatoform panic attacks do not necessarily predict nor are they solely in the province of panic disorder. Initial panic attacks are sometimes indicative of the early stages of psychiatric illness, particularly major depression. Additionally, in any given year, 8% to 10% of the American public will experience a simple panic attack that does not necessarily reflect morbidity or abnormality.^{1,8} Sometimes panic attacks result from anxiety disorders such as obsessive-compulsive disorder (OCD) or posttraumatic

stress disorder (PTSD). Some patients experience panic attacks in social settings that are triggered by discomfort or embarrassment associated with social interactions. Such patients would most likely be experiencing panic attacks stemming from social anxiety disorder rather than panic disorder. Panic attacks associated with panic disorder are generally triggered randomly, although they may occur at times when the individual is under stress. The initial attack may eventually lead patients to fear similar settings because they worry that such a setting may trigger a subsequent attack, but the classification of panic disorder is only appropriate when the fear of future attacks substantially changes patients' behavior due to an effort to reduce the likelihood of another attack.

Primary care physicians often see patients who have just experienced their first panic attack because the physical symptoms have disturbed them, whereas psychiatrists frequently see patients who have developed phobic avoidance of places and things they think trigger the attacks. Specific diagnostic criteria (Table 1) can aid primary care physicians in diagnosing panic disorder. First, for the DSM-IV criteria for panic disorder to be met, a patient must have had recurrent, unexpected panic attacks followed by at least 1 month of persistent concern about another attack, worry about possible implications or consequences of panic attacks, or significant behavioral change related to attacks. Second, the patient may or may not have agoraphobia. Third, the panic attacks are not the result of the psychological effects of a substance or medical condition, and, finally, the attacks will not be better accounted for by another mental disorder such as panic attacks as part of PTSD or major depression.

TREATMENT OPTIONS

Appropriate treatment for patients with panic disorder will improve quality of life and productivity as well as reduce health care costs.⁹ It is important to convey hope of expected improvements to patients newly diagnosed. In addition to educating patients about panic disorder and available treatments, one of the most essential first steps to treatment is providing general lifestyle recommendations to patients, especially diagnosis-naïve patients. Patients can improve their condition by avoiding caffeine, limiting alcohol and nicotine, and exercising regularly. Emphasizing the importance of adherence to treatment is also critical to patients, particularly those worried about becoming addicted to drug therapies or those concerned about side effects. Patients often think they can take medication only as needed. Instead, physicians should explain to patients that treatment of panic disorder requires a chronic disease model (such as a diabetic maintaining health and avoiding symptoms with regular insulin), rather than an acute symptom control model (a patient with a headache taking aspirin) or a panacea model (taking an antibiotic until the illness is completely cured). Physicians can also improve treatment

Table 2. Comparative Benefits of Medications for Panic Disorder^a

Benefit	High-Potency Benzodiazepines	TCAs	SSRIs
Rapidity of response	+++	+	+
Decrease panic attacks	+++	+++	+++
Decrease anticipatory anxiety	+++	+	+
Decrease phobic avoidance	++	+	++
Antipanic efficacy	+++	+++	+++
Antidepressant efficacy	0	+++	+++

^aBased on data from Rickels and Schweizer.¹⁶

Abbreviations: SSRI = selective serotonin reuptake inhibitor, TCA = tricyclic antidepressant. Symbols: + = mild, ++ = moderate, +++ = marked, 0 = not present.

outcomes by helping patients develop coping strategies and by explaining the prognosis and etiology of panic disorder to family members. Research indicates that general counseling by primary care physicians for mood and anxiety disorders can have a moderate to significant impact on patient outcome.¹⁰

PHARMACOTHERAPY

Pharmacotherapy is the mainstay treatment for panic disorder in the primary care setting. In selecting a pharmacologic treatment, clinicians need to adhere to specific treatment criteria: early- and late-stage side effects should be minimized, as should the potential for problematic drug interactions, and the treatment should be relatively easy to administer as well as acceptable to the patient and physician for long-term use.

In panic disorder, agents from several classes may be used as monotherapy or in combination. Among them are selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants (TCAs), and benzodiazepines (preferably long-acting). The SSRIs paroxetine and sertraline and the benzodiazepines alprazolam and clonazepam have been approved for the treatment of panic disorder by the U.S. Food and Drug Administration. Although medications such as bupropion, trazodone, buspirone, antipsychotics, and β -blockers might control specific anxiety symptoms, studies¹¹⁻¹⁵ have indicated that these medications are generally not appropriate monotherapies for panic disorder. SSRIs, TCAs, and benzodiazepines offer roughly comparable efficacy during short-term treatment for panic disorder; all markedly reduce the number and frequency of panic attacks (Table 2).¹⁶

SSRIs and TCAs also have antidepressant efficacy and therefore are more effective as monotherapy for treating comorbid depression (including euthymic patients at risk for recurrence due to a history of depression) and panic disorder, although many physicians view TCAs as secondary or tertiary agents because of their relatively negative side effect profile. The various SSRIs are structurally distinct and differ in pharmacokinetic profiles and rates of specific

Table 3. Comparative Risk of Side Effects Among Treatments for Panic Disorder^a

Side Effect	High-Potency Benzodiazepines	TCAs	SSRIs ^b
Short-term treatment			
Sedation and psychomotor impairment	++	++	0/+
Anticholinergic effects	0	+++	+
Orthostatic hypotension	0	++	0
Hypertensive reactions and dietary restrictions	0	0	0
Hyperstimulation	0	++	+ / ++
Long-term treatment			
Physical dependence	++	0	0
Discontinuation symptoms	+++	+	++
Risk of abuse	+	0	0
Weight gain	0	++	0
Sexual dysfunction	+	+	++

^aAdapted with permission from Rickels and Schweizer.¹⁶

^bNo data from controlled long-term studies available.

Abbreviations: SSRI = selective serotonin reuptake inhibitor, TCA = tricyclic antidepressant. Symbols: + = mild, ++ = moderate, +++ = severe, 0 = not present.

side effects.¹⁷ Also, physicians should monitor for drug interactions especially with the SSRIs fluoxetine, paroxetine, and fluvoxamine in patients taking warfarin, codeine, β -blockers, or other agents.

Advantages that benzodiazepines used as monotherapies have over SSRIs are rapid onset, low cost, and high patient acceptance. Additionally, the comparative risks of anticholinergic effects, orthostatic hypotension, weight gain, hyperstimulation, sexual dysfunction, and sedation/psychomotor impairment are considerably lower with benzodiazepines than with TCAs, and benzodiazepines are associated with fewer sexual adverse events than SSRIs (Table 3).¹⁶ However, depression can be exacerbated with benzodiazepines, and they are associated with sedation and psychomotor and cognitive impairment (particularly in older patients and if used intermittently). Additionally, benzodiazepines may induce withdrawal reactions when discontinued, and, although the risk is relatively low, the potential exists for abuse, especially in polysubstance abusers. If benzodiazepine treatment is chosen, a long-acting agent should be used. SSRIs have the broadest range of indications and may be the best choice if the patient with panic disorder has another comorbid disorder.

Several studies have been conducted to test the efficacy of various agents in treating panic disorder. Ballenger et al.¹⁸ examined 425 patients with DSM-III-R panic disorder with or without agoraphobia who underwent a 2-week drug-free washout period to determine the minimum paroxetine dose effective for treating panic disorder. Study results indicated that paroxetine was an effective and well-tolerated short-term treatment of panic disorder with an optimal dose of 40 mg/day. In a 12-week study of sertraline and paroxetine in panic disorder, Bandelow¹⁹ reported that both agents effectively reduced panic attacks and associated agoraphobia, anticipatory anxiety, disability, and health worries in

patients. In a study of escitalopram in the treatment of 360 patients with panic disorder, Stahl et al.²⁰ reported that escitalopram was more efficacious than citalopram and placebo on measures of treatment response.

Investigations examining the effectiveness of benzodiazepines include a multicenter, double-blind, placebo-controlled study by Moroz and Rosenbaum²¹ that evaluated the efficacy and safety of clonazepam in the treatment of panic disorder and assessed the tolerability of a schedule for gradual discontinuation. They found that clonazepam was an efficacious and safe short-term treatment for panic disorder. They also reported that discontinuance during and after slow tapering was well tolerated. Other long-term studies of benzodiazepines for treating panic are discussed by Doyle and Pollack²² elsewhere in this supplement.

Cognitive-behavioral therapy (CBT) should be considered by primary care physicians as a possible referral option for patients who prefer nonpharmacologic therapy, need help discontinuing medication, or have refractory symptoms, persistent cognitive factors, contributing behavioral patterns, anxiety sensitivity, or comorbid conditions. CBT can be effective not only as monotherapy but also as adjunctive therapy to pharmacotherapy to increase patients' long-term functioning (see the article by Otto²³ elsewhere in this supplement).

EFFECTIVE MANAGEMENT OF PANIC DISORDER IN PRIMARY CARE

Physicians can take many steps to improve the management of panic disorders (as well as other mood and anxiety disorders) and thereby achieve better long-term outcomes. First, patient engagement is critical. Patients need to not only understand and accept the diagnosis, but they should be and should feel that they are an active part of treatment decisions. Enabling patients to voice preferences and concerns regarding treatment options can aid in this task. Early telephone support encouraging patient adherence is also very helpful for patients with panic disorder since they often need support due to their pronounced sensitivity to symptoms.

When first prescribing treatment, primary care physicians should present the patient with the following 5 medication messages demonstrated to improve adherence: (1) take the medication every day, (2) allow 2 to 4 weeks for results, (3) continue taking the medication even if improvement occurs, (4) do not discontinue it without contacting the physician, and (5) call the physician with any treatment-related problems. Primary care physicians then should carefully monitor the initial stages of pharmacotherapy because patients frequently neglect to fill their prescriptions, and, of those patients who do, many do not take the first dose. Long-term monitoring of dose and response is also important.

Another important step in managing panic disorder is for primary care physicians to ensure that a patient receives ad-

equated treatment. To accomplish this, physicians not only must select a medication that is effective, but should titrate to a dose that is adequate as well. Additionally, if psychotherapy is chosen as a course of treatment, then the same standard should apply; the physician should recommend a psychotherapeutic approach that is appropriate as well as affordable, remembering that in panic disorder, simple, supportive psychotherapy is likely to be ineffective. Monitoring therapy, and increasing dose, switching, or augmenting therapy as dictated by the patient's response is critical to successful treatment.

Supplemental treatment with benzodiazepines can improve incomplete responses with serotonergic antidepressants and/or CBT to achieve complete remission. Long-term treatment success depends on providing therapy for at least 1 year, or longer if necessary. To discontinue benzodiazepine or SSRI treatment, doses should be tapered to lessen rebound or withdrawal; use of newer extended-release formulations may also help.

Physicians also need to be aware of what factors might contribute to treatment nonadherence in order to become more adept at identifying patients who are potentially at risk. Grilo et al.²⁴ conducted a collaborative panic treatment study to examine what pretreatment factors were associated with attrition. Six domains (demography, panic disorder severity, psychiatric comorbidity, illness/treatment attributions, coping styles, and personality styles) were used to predict attrition in 162 patients who were given 11 visit-treatments. By the end of the study, 40 patients had discontinued treatment, and final multivariate regression analyses revealed that lower household income, pessimistic treatment attitudes, attributing the panic disorder to life stressors, and older age were associated with dropping out. Other reasons for nonadherence include recovery (in the context of the acute illness model, in which patients stop taking medication after a short time), fear of becoming dependent on the medication, and negative prior personal or familial medication experiences.

Treatment intolerance also can decrease patient adherence; however, with benzodiazepine treatment, intolerance is not common. Treatment intolerance occurs with the SSRIs but less often than with TCAs due to their better side effect profile. Cowley et al.²⁵ conducted a study assessing reasons for pharmacologic treatment failure in 106 patients with panic disorder and reported that although ineffective medications or inadequate trials were important, the most common reason was side effects, especially with TCAs.

To minimize treatment intolerance, primary care physicians should initiate treatment at a low dose (half the usual starting dose used in depression is reasonable). To combat treatment-resistance, physicians may prescribe CBT, inquire about and provide support related to life stressors (e.g., marital conflict, divorce), provide education to avoid anxiogenic health habits (e.g., caffeine or alcohol consumption, frequent use of over-the-counter cold medications, inad-

equate sleep or exercise), and rule out substance abuse or other psychopathologies such as bipolar depression, phobia, or personality disorder.

Exercise can be as effective as medication in reducing panic attacks and anticipatory anxiety.²⁶ Although some patients with panic disorder resist exercise due to a fear of stimulating an attack, studies have found that exercise does not cause panic attacks in most patients with panic disorder. In fact, Martinsen et al.²⁷ found that of 35 patients with panic disorder who completed supramaximal exercise and experienced high values of blood lactate during the supramaximal test, only 1 experienced a panic attack. Additionally, patients who do not exercise have higher heart rates than those who do.²⁸ Therefore, patients should be encouraged to engage in some form of regular exercise, and those who may be avoiding exercise out of fear of triggering an attack should be educated that regular exercise can reduce the frequency of panic attacks, relieve tension, and improve sleep.

Finally, primary care physicians should develop collegial collaborative relationships with psychiatrists. Katon et al.²⁹ randomly assigned 115 primary care patients with panic disorder to a collaborative care intervention consisting of systematic patient education and 2 visits with a consulting psychiatrist and compared the outcome with that of usual primary care. Study results indicated that patients who received collaborative care experienced a mean of 74.2 more anxiety-free days during the 12-month intervention. The distribution of the cost-effectiveness ratio based on total outpatient costs suggested a 70% probability that the intervention had lower costs and greater effectiveness compared with usual care.

All of these steps can help primary care physicians improve long-term outcomes for patients with panic and other mood or anxiety disorders by ameliorating disease symptoms, promoting patients' productivity and financial stability, and empowering them to actively participate in their own treatment. As a consequence, patients may develop an improved sense of overall emotional and physical well-being and quality of life.

Drug names: alprazolam (Xanax and others), bupropion (Wellbutrin and others), buspirone (BuSpar and others), citalopram (Celexa), clonazepam (Klonopin and others), escitalopram (Lexapro), fluoxetine (Prozac and others), paroxetine (Paxil and others), sertraline (Zoloft), trazodone (Desyrel and others), warfarin (Coumadin, Jantoven, and others).

Disclosure of off-label usage: The author has determined that, to the best of his knowledge, citalopram and escitalopram are not approved by the U.S. Food and Drug Administration for the treatment of panic disorder.

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