Recognizing anxiety disorders

Abstract: The majority of patients with anxiety disorders present in primary care settings, and many are undiagnosed or undertreated—each disorder has defining characteristics. Anxiety disorders are debilitating, and proper treatment can improve quality of life. Preferred treatments are cognitive-behavior therapy and pharmacotherapy with selective serotonin reuptake inhibitors.

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It is estimated that at least 60% of patients with symptoms of anxiety disorders seek treatment in a primary care setting, often with medically unexplained symptoms; anxiety is a universally experienced response to stress. However, when feelings of anxiety are excessive, or occur in the absence of a stressor and significantly interfere with a person’s functioning, they are considered pathologic and are diagnosed as an anxiety disorder.

These are the most common psychiatric disorders and frequently occur along with other physical or psychiatric illnesses. The majority of people with one anxiety disorder will also have another, and people that suffer from them will also frequently experience depressive disorders or substance abuse.

It is estimated that approximately 40 million American adults (or 18% of the population) experience an anxiety disorder in a given year; they are more common in people under 65 years of age. In addition, social phobia and obsessive-compulsive disorder (OCD) have a typical onset in adolescence.

Key words: anxiety disorders, panic disorder, phobia, social anxiety disorder, obsessive compulsive disorder, posttraumatic stress disorder, generalized anxiety disorder
Recognizing anxiety disorders in the primary care setting is the first step to providing treatment, limiting disability, and improving a patient’s quality of life. However, evidence suggests that even when primary care patients are accurately diagnosed with anxiety disorders, there are important gaps in the mental healthcare that they receive. These gaps include infrequent referrals or recommendations for psychotherapy and an evidence-based, effective intervention to treat anxiety disorders.  

### Types of anxiety disorders

There are essential features that distinguish the various anxiety disorders. Each of them center on an experience of irrational and disproportionate fear or dread. Whether the symptoms are physiologic (palpitations, excessive sweating) or psychological (the experience of intrusive, disturbing thoughts), the underlying precipitant is fear.

The American Psychiatric Association recognizes the following primary anxiety disorders:

- **Panic disorder (PD)** is characterized by recurrent, unexpected panic attacks followed by at least 1 month of persistent concern about having another. The panic attacks can vary greatly in frequency, and patients may go for weeks to months without one only to have them resume again. Symptoms may resemble an acute cardiac event with sweating, palpitations, shortness of breath, choking sensation, chest pain, nausea, and lightheadedness. PD can occur with or without agoraphobia. A person with agoraphobia fears being unable to escape should a panic attack occur. The fear is not related to the situation, it is of having a panic attack, being out of control, and helpless. Agoraphobia can occur in people who have never actually had a panic attack.

- **Specific phobia** is marked by persistent, irrational fear of a particular object, place, or situation referred to as a phobic stimulus. Patients will seek treatment when the fear interferes significantly with their daily routine, occupation, or social functioning; exposure therapy is usually effective.

- **Social phobia or social anxiety disorder (SAnD)** refers to a fear of social or performance situations (such as public speaking) in which embarrassment may occur, resulting in an immediate anxiety response; the fear relates to being judged or humiliated. It can be distinguished from shyness based on the degree of discomfort and social/work impairment that results from the anxiety. Social phobias are self-reinforcing in that the anxiety about performing interferes with performance—leading to embarrassment—which further reinforces the fear of performing.

- **Obsessive-compulsive disorder (OCD)** is characterized by obsessions (repetitive, intrusive thoughts) and by compulsions (repetitive, ritualistic behaviors). Patients may experience either obsessions, compulsions, or both. The thoughts or obsessions cause anxiety, which is partly relieved by the compulsive, ritualistic behavior. The patient may spend great amounts of time carrying out rituals or may go to great lengths to avoid situations associated with the obsessions. Although aware of the irrational nature of the thoughts and behaviors, people with OCD feel helpless to interrupt the cycle.

- **Posttraumatic stress disorder (PTSD)** follows a traumatic event. The event does not have to be personally experienced or witnessed to have a traumatic effect. Sometimes the patient develops anxiety related to an event that was experienced by someone else and then made known to them. The presenting symptoms include depression, anxiety, sleep disturbances, sexual dysfunction, or even psychosis. Intense re-experiencing through traumatic memories is most common and can involve flashbacks or hallucinations. People often go to great lengths to avoid anything that reminds them of the trauma. In PTSD, symptoms appear more than 1 month after exposure. If the symptoms appear within 1 month after the traumatic event, a diagnosis of acute stress disorder (ASD) may apply. If unresolved, ASD can progress to PTSD.

- **Generalized anxiety disorder (GAD)** is one of the most common psychiatric disorders in primary care, although it is often undertreated or unrecognized. It is characterized by uncontrollable anxiety over a period of at least 6 months. Symptoms include restlessness, fatigue, difficulty concentrating, irritability, difficulty sleeping, and muscle tension. In primary care, the patient may present with unexplained physical symptoms or may have anxiety in the presence of a medical condition. GAD has been linked to heart disease, gastrointestinal disturbances, and pain disorders.

### Understanding the causes

The development of anxiety disorders can be attributed to a combination of neurobiologic, genetic, and environmental factors. Complex interactions of various neurotransmitters, specifically an underactivation of the serotonergic system, an overactivation of the noradrenergic system, a dysregulation of cortisol, and a decrease in gamma-aminobutyric acid, are the major inhibitory neurotransmitters that are implicated in anxiety disorders.
PD, GAD, phobias, and OCD all have significant familial occurrence.4,11–13 Twin studies, though small in size, provide evidence of a genetic contribution to PTSD.14,15 Early childhood trauma is a significant environmental factor in the development of anxiety disorders.16

**Diagnosis and assessment**

The initial assessment of a patient with a new onset of anxiety includes a physical exam, a mental status exam, a medical and psychiatric history, family history of anxiety or mood disorders, and a basic lab profile. If the probability of a medical disorder is low (lack of physical findings, younger age, or typical anxiety disorder presentation), initial lab studies might be limited to the following:

- complete blood cell count
- chemistry profile
- thyroid function tests
- urinalysis
- urine drug screen.

In older patients with abnormalities on physical exam and an atypical presentation of the anxiety disorder, additional clinical tests such as an ECG, electroencephalogram (EEG) magnetic resonance imaging, lumbar puncture, and HIV testing could rule out cardiac, cerebral, or infectious processes.1,17 The specific workup is based on the patient’s presentation and history. Attention must be given to the detection of any medical condition that may be the cause of the anxiety symptoms. (See Examples of medical conditions that may cause anxiety symptoms.) Similarly, somatic symptoms such as headaches or sleep disturbances may relate to anxiety.18 Practitioners should ask about past or present abuse, which is known to contribute to the development of anxiety disorders.19,20

Assessment includes a review of current medications, use of alcohol and other substances, herbal preparations, and over-the-counter (OTC) drugs. Anxiety symptoms can be related to the physiologic effects of caffeine, abusive drugs, a prescribed or OTC medication, or a toxin; alcohol and drug abuse is relatively common in patients with SAnD.21 Sympathomimetics, antihypertensives, and nonsteroidal anti-inflammatory drugs (NSAIDs) are among the prescription medications that may cause anxiety symptoms.1 Suspected medications can be tapered and withdrawn while observing the patient for a decrease in anxiety symptoms. Treatment of anxiety disorders in the presence of substance abuse should be coordinated with an addiction specialist.22

All patients should be asked directly about suicidal and homicidal ideation, and if present, a clinical determination would need to be made regarding necessary intervention. If a patient expresses active suicidal or homicidal ideation, immediate intervention is needed, and hospitalization may be required. Patients with anxiety symptoms should be assessed for depression, which can be present in up to 50% of patients with an anxiety disorder—especially in those with GAD or SAnD.23,24 A failure to diagnose and treat the depression or other primary psychiatric disorders can exacerbate secondary anxiety symptoms. If the symptoms exist in the context of a depressive disorder, antidepressant therapy will very likely improve the anxiety. However, if depression follows or is comorbid with the anxiety disorder, both conditions may be more difficult to treat and may result in a poorer prognosis for the patient.24

Psychosocial assessment should explore why the patient is seeking help at this particular time. Specific information as to how the anxiety has affected the person’s relationships, along with occupational and social functioning, will help both the nurse practitioner (NP) and the patient understand his or her motivation for treatment. Involving a patient in a discussion about the problem helps to establish him or her as an active participant in the treatment process; this subsequently increases a sense of personal control, contributes to self-esteem, and fosters independence. It further provides an opportunity for the clinician to gather information regarding the patient’s attitude toward treatment options, thus facilitating an acceptable course of action.

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**Examples of medical conditions that may cause anxiety symptoms**

<table>
<thead>
<tr>
<th>System</th>
<th>Medical Disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>Pulmonary embolism</td>
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<tr>
<td></td>
<td>Myocardial infarction</td>
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<tr>
<td></td>
<td>Heart failure</td>
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<td></td>
<td>Cardiac dysrhythmia</td>
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<tr>
<td>Endocrine</td>
<td>Hyperthyroidism</td>
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<td>Hypothyroidism</td>
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<td>Hypoglycemia</td>
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<td></td>
<td>Pheochromocytoma</td>
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<td></td>
<td>Hyperadrenocorticism</td>
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<tr>
<td>Metabolic</td>
<td>Porphyria</td>
</tr>
<tr>
<td></td>
<td>Vitamin B&lt;sub&gt;12&lt;/sub&gt; deficiency</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Hyperventilation</td>
</tr>
<tr>
<td></td>
<td>Chronic obstructive pulmonary disease</td>
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<tr>
<td></td>
<td>Pneumonia</td>
</tr>
<tr>
<td>Neurological</td>
<td>Encephalitis</td>
</tr>
<tr>
<td></td>
<td>Vestibular disturbances</td>
</tr>
<tr>
<td></td>
<td>Neoplasm</td>
</tr>
</tbody>
</table>


The following questions and statements can help promote discussion:

- When were you first aware of feeling anxious?
- Tell me what was happening in your life at that time.
- Can you describe what “anxious” feels like for you?
- Was there (or is there) a particular event that triggered (or triggers) the symptoms?
- What have you done to lessen the anxiety? Have these measures helped?
- In what ways has the anxiety changed your life?
- Do you experience any other symptoms that create discomfort such as headaches or trouble sleeping?

If the patient describes a sense of fear and a pattern of avoidance, the nature of the fear can help identify the disorder. Is there a fear of having a panic attack, or is there a fear of being embarrassed, helpless, or losing control? Is the fear related to a specific object or situation? Is the situation related to times when the patient feels judged? Clinicians may consider using a standardized tool to measure anxiety such as the Generalized Anxiety Disorder Severity Scale (GADSS),23 the GAD-7, or the shorter GAD-2, which perform well for detecting GAD, PD, PTSD, and SAnD.26 The need for and type of treatment are determined by the severity of symptoms, the presence of a comorbid mental disorder/physical illness, the level of disability and its impact on social functioning, concomitant medication, and a history of good response/poor tolerance from previous treatment approaches.24

In addition to the clinical determinants described above, the patient’s attitude toward treatment approaches and willingness to accept the clinician’s recommendation are essential factors to be considered when planning care. The NP can assist the patient to recognize strengths and resources that will support treatment; this can be caring family or friends, community supports, personal accomplishments, or past success in dealing with stressful life events. Through this discussion, the nurse helps counter the patient’s negative personal view and sense of hopelessness, which contributes to the patient’s self-esteem.

**Pharmacological treatment-SSRIs**

Selective serotonin reuptake inhibitors (SSRIs) are the primary pharmacologic treatment for anxiety disorders based on their efficacy and tolerability;22,24,26-28 they have the added advantage of treating comorbid mortality with a low risk of mortality on overdose. SSRI medications are prescribed on a routine (not p.r.n.) basis in the same dosages as used to treat depression. It is recommended to start at a low dose, and increase to a therapeutic dose. This is especially important when treating older adults or medically compromised patients who may excrete the medication slowly.21 All patients should be monitored for suicidal ideation—especially at the beginning of treatment. If drug treatment is considered for children and adolescents, the SSRIs (at lower doses) are the first-line based on limited evidence.23,24 It should be noted that the SSRIs carry a black box for suicidal ideation in children, adolescents, and young adults.

The SSRIs typically produce an increase in anxiety during the initial days or weeks of treatment; patients should be made aware of this before starting the medication. A benzodiazepine, as needed, can help relieve the feelings of jitteriness during this period. Advise the patient that it may take up to 4 weeks to begin to feel the therapeutic effect of the medication, and 12 weeks must be allowed to fully evaluate the drug’s effectiveness.21,24 The typical course of treatment involves maintenance therapy for at least 6 to 12 months.8,24,29 In the treatment of GAD, evidence is particularly strong that continuing SSRIs for at least 12 months is necessary to achieve maximum benefit and to ensure sustained improvement.31 When discontinuing antidepressants, the clinician should taper the drug over the course of several weeks to minimize the likelihood of discontinuation syndrome.31 This can cause a number of very uncomfortable symptoms including lightheadedness, sleep disturbance, headache, and can be confused with relapse. Discontinuation syndrome is more likely to occur with short-acting SSRIs such as paroxetine, sertraline, and fluvoxamine, and less likely to occur with an SSRI with a long half-life such as fluoxetine.32

The choice of SSRI depends on the condition being treated. There is good evidence for SSRIs being effective across the disorders, but some appear to be better than others in treating specific disorders. (See Use of SSRIs in treatment of anxiety disorders.)

Most anxiolytic medications are well tolerated, but anxious patients are particularly prone to experience adverse reactions.27 Common adverse reactions with the SSRIs are nausea, dizziness, headaches, jitteriness, and sleep disturbances;27,32 hyponatremia is a risk particularly seen in the elderly.27 Sexual dysfunction occurs in 17% to 41% of patients and often becomes less of a problem as the body adjusts to the medication.33,34 Usually, this can be managed by adjusting the dose or switching to another SSRI medication.
Another strategy is to use a once-a-day dosing schedule, which will allow the patient to plan sexual activity before taking the medication.

There is no evidence that combining SSRIs or increasing dosage improves treatment outcome.\textsuperscript{21,35} However, an exception is in the treatment of OCD, where higher than usual doses may be beneficial.\textsuperscript{24,35} If the patient does not respond to the SSRI medication after 12 weeks, options include switching to a different SSRI, increasing the dose of the current SSRI (although there is little evidence that this is effective except in the treatment of OCD), adding psychological therapy, or switching from an SSRI to another category of medication.\textsuperscript{21,30}

\section*{SNRIs}
The majority of studies regarding serotonin-norepinephrine reuptake inhibitors (SNRIs) in the treatment of anxiety disorders are based on venlafaxine (Effexor) which is FDA approved for the treatment of GAD, PD, and SAnD; Duloxetine (Cymbalta) has FDA approval for the treatment of GAD. In addition, there is evidence that both medications are effective for relapse prevention of GAD.\textsuperscript{32} The SNRIs have a similar adverse reaction profile to SSRIs and can also produce a discontinuation syndrome during tapering or times of nonadherence.

\section*{TCAs}
Tricyclic antidepressants (TCAs) can also be used in the treatment of anxiety disorders. However, the combination of cardiotoxicity, lethality of overdose, and bothersome anticholinergic adverse reactions make TCAs a second-line treatment for patients with intolerance for, or an inadequate response to, SSRIs. Evidence supports the use of imipramine (Tofranil) in the treatment of PD, PTSD, and GAD, but TCAs are not effective in the treatment of SAnD.\textsuperscript{23} Clomipramine (Anafranil) is the only TCA with FDA approval for the treatment of anxiety disorders, and the approval is specifically for the treatment of OCD; it is the only TCA useful in the treatment of OCD.\textsuperscript{3,37} As with SSRIs, dosing should start low and gradually be increased, treatment effect will take several weeks, and a benzodiazepine may curb the initial increase in anxiety. Orthostatic hypotension related to TCAs increases the risk of falls—a particular concern with older adults.

\section*{MAOIs}
The monoamine oxidase inhibitor (MAOI), phenelzine (Nardil) has shown to be effective in the treatment of PD and SAnD. However, the adverse reactions, along with the potential for significant food and drug interactions associated with MAOIs, make them a second-line treatment. To avoid serotonin syndrome, it is recommended that patients wait 5–to-6 weeks after discontinuing an SSRI with a long half-life (fluoxetine). Patients can also wait 2 weeks after discontinuing a drug with a short half-life (paroxetine, fluvoxamine, or the TCAs) before beginning treatment with an MAOI.\textsuperscript{21} The MAOIs are not FDA approved for the treatment of anxiety disorders.

\section*{Benzodiazepines}
Benzodiazepines have a fast-acting anxiolytic and sedating effect, therefore, they are the drug of choice for immediate relief of symptoms associated with severe anxiety.\textsuperscript{37} The following benzodiazepines are FDA approved for the treatment of anxiety, nervousness, and tension associated with anxiety.

\begin{table}[h]
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\begin{tabular}{|l|l|l|l|}
\hline
\textbf{SSRI} & \textbf{Daily Dose Range/Max} (Adult < 65 yrs, without renal or hepatic impairment) & \textbf{Disorder (± indicates FDA approval for specific disorder)} & \textbf{Common Brand Name} \\
\hline
Citalopram & 20–40 mg & PD, SAnD & Celexa \\
Escitalopram & 10-20 mg & PD, SAnD, PTSD, OCD, GAD± & Lexapro \\
Fluoxetine & 20–60 mg & PD±, SAnD±, PTSD±, OCD± & Prozac \\
Fluvoxamine & 50–250/300 mg & PD, SAnD±, PTSD±, OCD± & Luvox \\
Paroxetine & 10–60 mg & PD±, SAnD±, PTSD±, OCD±, GAD± & Paxil \\
Sertraline & 25–150/200 mg & PD±, SAnD±, PTSD±, OCD±, GAD & Zoloft \\
\hline
\end{tabular}
\caption{Use of SSRIs in treatment of anxiety disorders}
\end{table}

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Symptom relief is not immediate, as is the case with benzodiazepines, and the therapeutic effects may not be felt for several weeks. Because benzodiazepines lower the response to buspirone, they have a limited role in treating anxiety symptoms, pending achieving a therapeutic effect from buspirone.

■ Antiepileptics
Pregabalin (Lyrica) has strong evidence (level I) of effectiveness in the treatment of GAD, while both pregabalin and gabapentin (Neurontin) have level II evidence for the treatment of SAnD. However, antiepileptics do not have FDA approval for the treatment of anxiety disorders. In addition, limited research in this area has resulted in few clear indications for their use, except as second-line or adjunctive therapy. NPs and patients should be aware that antiepileptic therapy is associated with an increased risk of suicidal thoughts and behaviors.

■ Other medications
The beta-blocker propranolol (Inderal) is effective in relieving symptoms related specifically to symptoms of performance anxiety, but there is no evidence of benefit in treating other symptoms of SAnD or any other anxiety disorders. Recent work has also shown the effectiveness of prazosin (Minipress), an alpha-blocker, in the treatment of nightmares related to PTSD. Neither of these medications have FDA approval for the treatment of anxiety disorders.

■ CBT
Cognitive-behavior therapy (CBT) is an established, evidence-based treatment and can be as effective as drug therapies in regards to anxiety disorders. In the absence of depression, CBT should be considered first-line treatment where accessible, acceptable to the patient, and appropriate to the severity of impairment. There is evidence that anxious patients may prefer psychological interventions over medication, and psychological therapy is considered first-line treatment with children and adolescents.

CBT helps patients alter the thought processes that support their fears, and at the same time, learn new skills and behaviors to better manage situations that provoke anxiety; this process may reduce the risk of relapse. CBT strategies include psychoeducation, self-monitoring, cognitive restructuring, somatic exercises, and exposure to feared stimuli. CBT typically extends over a 12- to 20-week period, although longer treatment may be necessary to maintain an initial response. Group therapy is especially effective for SAnD. There is evidence that the benefits of CBT last longer than those of medication for people with PD and perhaps also for OCD, PTSD, and SAnD. Access to this effective therapy has been limited to some extent by the lack of clinicians trained in CBT; the introduction of computer-assisted CBT programs will help make this treatment more available. However, it is uncertain whether there is an added benefit from combining psychological and pharmacologic therapies. The current recommendation is to use one or the other treatment initially and augment as indicated based on the patient’s response.

■ Course of treatment
During the initial treatment period, it is helpful to monitor patients regularly to assess their response to treatment and/or the experience of adverse reactions including suicidal thoughts; this can be accomplished via weekly visits or telephone contact. It is important to review the prescribed medication schedule, especially with patients who are on p.r.n. benzodiazepines, since there is a risk of substance abuse. After the patient has experienced a positive response
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