JAMA Internal Medicine | Review

Treatment of Anxiety for Adults in Primary Care Settings
A Review

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IMPORTANCE Anxiety disorders and symptoms are prevalent and burdensome, and patients are most likely to seek treatment in primary care settings. However, anxiety is underdetected and undertreated. This narrative review details behavioral and pharmacological treatment options that are feasible and effective in primary care.

OBSERVATIONS Screening for anxiety is recommended for primary care patients younger than 65 years. Given that anxiety often involves somatic symptoms, assessment should include patient-reported symptom measures, clinical interview, physical examination, and appropriate laboratory tests. For subthreshold symptoms (those that do not meet diagnostic criteria for anxiety disorders) and adjustment-related anxiety, starting with self-help and behavioral treatment is recommended. When deciding between behavioral, pharmacological, or combined treatment for anxiety disorders, consider the presentation, patient preferences, potential adverse effects, and treatment history, and engage in shared decision-making. Cognitive-behavioral therapy (CBT) is the first-line behavioral treatment for anxiety. Brief CBT in primary care delivered by embedded behavioral health clinicians is effective. First-line pharmacotherapy for anxiety disorders includes several selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors, which tend to be well tolerated without considerable long-term adverse effects. The main decision for pharmacological treatment is between a daily medication and a short-acting medication taken as needed for intermittent symptoms or while awaiting the effect of a daily medication. Benzodiazepines are not recommended due to risk of adverse effects, especially with long-term use. The Collaborative Care Management model, which involves collaboration between primary care clinicians, consulting psychiatrists, and care managers who monitor patient progress and provide behavioral treatment, improves anxiety outcomes compared to usual primary care.

CONCLUSIONS AND RELEVANCE Clinicians should recognize common anxiety presentations and understand how to differentiate between anxiety and other psychiatric or medical conditions. Referring patients to behavioral health specialists for CBT and/or prescribing recommended pharmacotherapy with Collaborative Care Management can help to reduce patient morbidity and improve functioning.

JAMA Intern Med. doi:10.1001/jamainternmed.2026.0395
Published online May 4, 2026.

JAMA Internal Medicine Patient Page

Supplemental content

CME at jamacmelookup.com

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Clinicians in primary care frequently manage patients with anxiety disorders, making it critical to understand evidence-based treatment options. Anxiety disorders, which include generalized anxiety disorder (GAD), panic disorder, agoraphobia, social anxiety disorder, and specific phobia, are the most common class of psychiatric disorders.[1] Subthreshold anxiety symptoms, which are clinically relevant but do not meet diagnostic criteria for anxiety disorders (eg, excessive worry for 3 months, not reaching the minimum duration of 6 months required for diagnosis of GAD[2]), are also common.[3] Anxiety disorders can result in functional impairment,[4] reduced quality of life,[5] and increased health care utilization,[6] and are a risk factor for suicidal ideation and attempts.[7]

Despite their prevalence and burden, anxiety disorders are underdetected and undertreated. Patients are more likely to seek treatment in primary care, rather than specialty mental health settings.[8] Fewer than half of anxiety disorder cases are correctly detected or diagnosed in primary care,[9] in part due to limited visit time. Patients may present with somatic symptoms that they do not recognize as related to anxiety, and the potential for comorbidity and complex reciprocal relationships between anxiety and medical illness can further complicate assessment.[10-12]

Among US primary care patients with anxiety disorders, only 40% receive potentially adequate behavioral or pharmacological treatment.[13] This review updates and extends previous reviews (eg, DeGeorge et al,[14] Szuhany and Simon[15]) following new United States Preventive Services Task Force (USPSTF) recommendations[16] to provide guidance on screening, diagnosis, and evidence-based behavioral and pharmacological treatment for a range of anxiety disorders and symptoms among adults in primary care settings.

Table 1. Prevalence and Common Features of Clinical Presentation for Adult Anxiety Disorders[a]

Disorder	Prevalence in primary care, %	Common features of clinical presentation
Generalized anxiety disorder	7.6	• Excessive, uncontrollable worry about numerous concerns along with ≥3 bodily (restlessness or feeling on edge, muscle tension, easily fatigued) or other (irritability, trouble sleeping, poor concentration) symptoms on more days than not for ≥6 mo • Concerns span a wide range such as finances, work responsibilities, health of self or family members, potential misfortune, getting routine tasks done, or minor matters • May report being a lifelong "worrywart" or having been a worrier as long as they can remember, even in childhood
Social anxiety disorder	6.2	• Intense fear of social or performance situations with concerns about embarrassment or scrutiny from others • Performance subtype if fear is related only to speaking or performing in public • Feared social situations almost always provoke an anxiety response out of proportion to the threat posed (based on clinician judgment) and are actively avoided or endured with intense fear or anxiety • Impaired normal routine or work/social functioning due to avoidance of social situations • May experience bodily symptoms (eg, blushing, sweating, trembling) during social interactions that are perceived as highly embarrassing and likely to attract others' attention • May report considerable mental energy spent on presituation anticipatory anxiety or postsituation processing of symptoms or others' reactions
Specific phobia	Not available	• Intense fear of a specific object or situation that is excessive or out of proportion to the danger posed (based on clinician judgment) • Subtypes include animal (eg, dogs), natural environment (eg, heights), blood-injection-injury (eg, needles), situational (eg, flying in airplanes), and other • Feared object or situation almost always provokes an anxiety response and is actively avoided or endured with intense fear or anxiety • May report a lack of current anxiety due to having rearranged daily life to minimize the chances of exposure to the feared object or situation
Panic disorder	6.8	• Recurrent panic attacks (with ≥4 physical or cognitive symptoms) with sudden onset of overwhelming fear or discomfort that reaches a peak within minutes • Physical symptoms such as heart palpitations, shortness of breath, chest pain, and feelings of being detached from oneself • Cognitive symptoms may include fear of dying and fear of losing control or "going crazy" • Panic attacks are unexpected (based on clinician judgment) with no obvious cue or trigger in the moment (eg, happens when relaxing) • ≥1 mo of persistent concern about panic attacks or behavior changes to avoid suspected triggers (eg, avoiding physical exertion, rearranging daily routine) • In extreme cases, may present repeatedly to emergency department with concerns of myocardial infarction or cardiac condition
Agoraphobia	Not available	• Marked fear that is out of proportion to the danger posed by real or anticipated exposure to ≥2 of the following: using public transportation, standing in line or being in a crowd, or being in open spaces, in enclosed places, or outside of the home alone • Can be diagnosed irrespective of meeting criteria for panic disorder • Fear is driven by thoughts that escape or assistance will be difficult if paniclike or embarrassing symptoms occur • Feared situation almost always provokes an anxiety response and is actively avoided, endured with intense fear, or requires a companion to be able to tolerate • May use safety behaviors (eg, self-medication) to endure feared situations or, in severe cases, be unable to work or rarely leave the home even for basic needs or events critical to functioning
Any anxiety disorder[b]	19.5	• Excessive fear (reaction to imminent threat) or anxiety (anticipation of future threat) and consequent behavioral disturbances such as persistent avoidance • Excessive worry or rumination regarding the anxiety-provoking stimuli and/or the implications of one's reaction to it • Persistent avoidance of feared object or situation, typically ≥6 mo (social anxiety disorder, specific phobia, agoraphobia) • Clinically significant distress or impairment in social, occupational, or other functioning • Symptoms not better explained by the symptoms of another mental disorder or a medical condition and not attributable to the physiological effects of a substance or medication

[a] This table highlights common features of each kind of anxiety presentation but does not list all the diagnostic criteria for each anxiety disorder. For full diagnostic criteria, see *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision*.[22]

[b] Common features listed are general across the various anxiety disorders.

Methods

This narrative review synthesizes findings from systematic reviews, meta-analyses, USPSTF guidelines, and treatment guidelines from professional organizations. We searched PubMed for anxiety reviews and guidelines published from 2005 to 2025 (see the eMethods in the Supplement for search terms). We supplemented this search with publications identified in reference lists of included articles and high-quality narrative reviews and randomized clinical trials (RCTs).

Epidemiology

Prevalence rates for US adult primary care patients are shown in **Table 1**. Lifetime prevalence of any anxiety disorder is more common among females (40.4%) than males (26.4%)[17] and less common among older adults (≥65 years).[18] Anxiety disorders tend to occur together and with depression. Among primary care patients with an anxiety disorder, 57% had at least 1 additional anxiety disorder, and nearly two-thirds also had major depressive disorder.[4] Substance use disorders are also common, with rates varying by di-

agnosis and reaching as high as 50%.[19] Finally, anxiety disorders co-occur with medical conditions, including chronic pain (50.4%), cardiovascular disease (32.5%-53.1%), asthma (11.8%-51.5%), chronic obstructive pulmonary disease (16%-30%), rheumatoid arthritis (25.9%-58%), gastrointestinal diseases (28%), and cancer (6.5%-30%).[11] Subthreshold anxiety symptoms are common in primary care patients,[3] associated with functional impairment,[20] and predictive of future anxiety disorder diagnoses.[21]

Clinical Presentation

Common features among patients experiencing clinically significant anxiety symptoms are presented in Table 1. Anxiety disorders broadly feature cognitive (eg, worry, fear), behavioral (eg, avoidance), and physiological (eg, trembling, muscle tension) symptoms. Specific anxiety disorders are differentiated by the types of situations that induce fear or anxiety (Table 1).[22] GAD is characterized by excessive, uncontrollable worry that spans multiple situations and domains of life (eg, work, relationships, school). Individuals with panic disorders fear having recurrent panic attacks (experience of intense fear and physical symptoms with an abrupt onset) and the physical, social, or mental health implications of panic attacks. Agoraphobia is characterized by a fear of specific places or situations outside an individual's home (eg, enclosed spaces, crowds, public transportation). With social anxiety disorder, the experience of anxiety is specific to social situations (eg, giving a speech, meeting new people). Specific phobia is characterized by intense fear of a specific object or situation (eg, heights, needles).

Assessment and Diagnosis

Assessment and diagnosis of anxiety are conducted through a combination of patient-reported symptom measures, clinical interview, physical examination, and at times, laboratory evaluation.

Screening

The USPSTF recommends screening for anxiety symptoms among adult primary care patients aged 64 years or younger, including those pregnant or post partum (strength of evidence: B recommendation).[16] Evidence is insufficient to recommend screening older adults.[16] The Generalized Anxiety Disorder-2, a 2-item patient self-report measure, performs well as an initial screening tool for any anxiety disorder[23]; patients scoring above the specified cutoff (≥3) should be evaluated further with a diagnostic interview combined with a validated symptom severity measure.[16,23] Further evaluation for those with positive Generalized Anxiety Disorder-2 screening results can be conducted with the Generalized Anxiety Disorder-7 (commonly known as GAD-7) scale,[24] a widely used, 7-item, free self-report measure of anxiety symptoms with good psychometrics in primary care.[25]

History of Present Illness and Differential Diagnoses

In response to a patient presenting with concerns of anxiety or a positive screening result on a validated anxiety screening tool, clinicians should assess symptoms (eg, type, frequency, intensity, duration), functional impairment (eg, home, social, work roles), predisposing factors (eg, family history), precipitating factors (eg, recent stressor), and perpetuating factors (eg, sleep or substance use patterns). Mood should be assessed given the association with depression[4] and bipolar disorder.[26] Suicidal ideation, intent, plan, and prior attempts should be assessed for safety reasons,[7] with appropriate follow-up as indicated.

Patients diagnosed in primary care are more likely to receive a diagnosis of anxiety not otherwise specified rather than specific diagnoses (eg, GAD).[27] These patients are less likely to receive mental health treatment than those who receive specific diagnoses; therefore, diagnostic specificity based on the anxiety disorders in Table 1 is preferred to the extent possible.[27]

In addition to differentiating among various anxiety disorder diagnoses, clinicians should consider other psychiatric diagnoses, including adjustment disorder, mood disorders, posttraumatic stress disorder, and obsessive-compulsive disorder. The presence of anxiety itself does not warrant an anxiety disorder diagnosis; anxiety is a universal, and, at times, adaptive human experience. Anxiety disorders can be differentiated from nonpathological anxiety—which involves transient, proportionate anxiety in response to life stressors (eg, feeling anxious for a few days while waiting for follow-up tests after abnormal laboratory test results)—by their persistence and the degree to which symptoms elicit distress and impair functioning. Subthreshold symptoms that persist (eg, several weeks to months) but do not meet full diagnostic criteria should be monitored, as they can cause impairment and progress to diagnosable disorders.[3,20,21] Adjustment disorder requires symptoms within 3 months of a specific precipitating event (eg, life stressor). The symptoms of depression and GAD have overlap (eg, trouble sleeping). Depression can be differentiated by low mood (feeling sad/hopeless) or loss of interest/pleasure unrelated to fear, whereas mania involves persistently elevated or irritable mood with symptoms such as flight of ideas and reduced need for sleep. Posttraumatic stress disorder can be differentiated by the experience of a traumatic event that threatens life or safety, trauma-related symptoms (eg, reexperiencing), and onset of symptoms temporally linked with the event that persist for longer than 1 month. Obsessive-compulsive disorder can be differentiated by persistent intrusive, unwanted obsessions and/or compulsions to engage in repetitive behaviors or mental acts. Primary care clinicians may be reluctant to assign diagnostic labels for anxiety; however, research shows primary care patients find diagnoses helpful and motivating to engage in treatment.[28]

In addition to differentiating between psychiatric diagnoses, consideration of other health conditions is vital. As an example, a patient with atrial fibrillation may report feeling anxious when they are in this rhythm, and treatment would then be to address the arrhythmia to relieve the anxiety. Additionally, co-occurring anxiety in the context of another health condition is a key factor in the differential diagnosis. The presence of a medical condition does not rule out an anxiety disorder unless the anxiety can be fully explained by the condition. For example, a patient with a pheochromocytoma may experience anxiety as a direct result of the tumor; being diagnosed with a tumor may also lead to anxiety about prognosis.[29] Treating the underlying tumor is important in both cases, but in the first case it may be curative of the anxiety, while in the second case, separate anxiety management would be beneficial. Lastly, some medications (eg, corticosteroids, sympathomimetics, stimulants) can lead to anxiety or anxiety-mimicking symptoms, either as adverse ef-

Table 2. Supporting Patient Self-Management of Anxiety

Strategy	Purpose/goal	Example talking points
Provide education	Help patient understand what is happening to them, share diagnosis, normalize, correct misperceptions, facilitate self-management by increasing knowledge, and establish rationale for treatment	• Anxiety is a normal, common experience many people deal with, and symptoms can include bodily sensations, worrying, panic attacks, and avoiding things • Anxiety spiral: there is a connection between thoughts, feelings, and behaviors; for example, if you have an anxious thought, you may then notice physical sensations of anxiety in your body, or vice versa, and then change your behavior in response to the anxious thoughts and feelings • A low level of anxiety can be adaptive, but anxiety becomes problematic when it is out of proportion, uncontrollable, or impairs daily functioning • You are reporting symptoms consistent with [patient's anxiety disorder], which often includes symptoms such as [common symptoms with patient's particular diagnosis] • Anxiety, including [patient's anxiety disorder] is highly treatable • Cognitive-behavioral therapy, or CBT, a goal-oriented talk therapy in which you examine connections between thoughts, emotions, and behavior patterns and develop new coping skills, is highly effective in treating anxiety • There are also many options for effective, safe medications that help with anxiety • What questions can I answer about anxiety or your treatment options?
Reinforce healthy self-management	Support patient's use of adaptive coping strategies	• What, if anything, are you currently doing to try to cope with the anxiety? • If healthy behaviors (eg, relaxation exercises, meditating, going for walks, seeking social support, journaling, faith-related coping, exposure to anxiety-provoking situations), reinforce patient's coping efforts • If unhealthy behaviors (eg, avoidance of anxiety-provoking situations, frequent "checking" behaviors, substance use to dull anxiety or facilitate sleep), discourage these behaviors by providing education on why they are problematic
Offer self-help resources	Facilitate adoption of helpful tools[a]	• Many people find it helpful to use anxiety-coping tools found in mobile applications, which have guided audio for practicing relaxation or mindfulness • Most of these kinds of applications have a free version; just be sure you use a reputable application such as Calm, Headspace, Breethe, Coping Coach, Mindfulness Coach, or Breathe2Relax • Some people like using tools found online through websites such as the National Alliance on Mental Illness (http://www.nami.org), Association for Behavioral and Cognitive Therapies (https://www.abct.org), or Substance Abuse and Mental Health Services Administration (https://www.samhsa.gov), or self-help books such as those recommended by the Association for Behavioral and Cognitive Therapies (https://www.abct.org/self-help-book-recommendations)

[a] Recommended resources are based on the authors' personal clinical experience as well as recommendations from relevant professional organizations.

fects or due to drug-drug interactions, so a thorough medication review and reconciliation should be conducted for possible contributors to anxiety.

Physical Examination

Patients who have anxiety may report physical symptoms such as chest pain, palpitations, tachycardia, or shortness of breath, and not report feeling anxious. While these symptoms are common in anxiety disorders, they are also common in other conditions. In evaluating a suspected anxiety disorder, after obtaining the history, the primary care clinician should consider a general physical examination to help rule out an underlying nonpsychiatric medical cause of symptoms. Common medical conditions leading to anxiety or anxiety-mimicking symptoms can be cardiac, pulmonary, and endocrine conditions, as well as substance use and cancers.[30,31] As an example, a patient reporting chest pain suspected to be anxiety should still undergo appropriate history, physical examination, and diagnostic testing for possible cardiac conditions. As another example, a patient reporting anxiety, heat intolerance, and tachycardia may benefit from having their reflexes checked and thyroid palpated as part of the physical examination for possible hyperthyroidism. Aquin et al[10] outline the mechanisms through which anxiety may increase risk for medical conditions, medical conditions may increase risk for anxiety, and anxiety and medical conditions may mutually maintain each other.

Laboratory Evaluation

Laboratory evaluation or electrocardiogram may be appropriate if there is concern for medical conditions that may contribute to or mimic anxiety. An example of this may be ordering thyroid tests in a patient presenting with anxiety, palpitations, sweating, and heat intolerance concerning for hyperthyroidism. A urine drug screen may be revealing if there is concern for underlying substance use contributing to the presentation. If test results are abnormal or point to a specific condition, further diagnostic testing and treatment of that condition are warranted.

Treatment Approach

A range of evidence-based behavioral and pharmacological anxiety treatments are recommended for use in primary care. When evaluating treatment options, it is critical to consider patient preferences, as the best treatment is one the patient will actually use. Patients who participate in shared decision-making or receive their preferred treatment have better treatment satisfaction, completion rates, and outcomes.[32] However, for subthreshold symptoms and adjustment-related anxiety, self-help and behavioral treatments are most appropriate, as there is not strong evidence for efficacy of pharmacologic treatment in these presentations.

Psychoeducation

Primary care clinicians should provide patients with general education about anxiety (**Table 2**), including normalizing it as a common experience; explaining the fight-or-flight response and the anxiety spiral or interconnected nature of thoughts, feelings, and behaviors; clarifying that low levels of anxiety are adaptive and thus the goal is not complete elimination of anxiety; and providing reassur-

ance that anxiety is highly treatable. Patients also need information regarding their specific anxiety diagnosis, such as common symptoms.

Patients value the opinion and recommendations of their primary care clinicians,[33] so clinicians explicitly encouraging self-management or formal treatment (as appropriate) can be powerful and motivating. Clinicians should reinforce patients' efforts at adaptive self-management of anxiety (Table 2), such as engaging in self-monitoring to understand their triggers, engaging in relaxation or mindfulness exercises, or challenging anxious thoughts, while discouraging unhealthy behaviors such as substance use and avoidance. Research has demonstrated the benefits of self-monitoring,[34] relaxation,[35] mindfulness,[36] and cognitive therapy[37] for anxiety. A Delphi study including both patients with anxiety and expert clinicians or researchers identified these types of evidence-informed self-management strategies as both feasible and effective for patients to use on their own.[38] In some cases, such as with subthreshold or mild symptoms or adjustment-related symptoms tied to a situational trigger, self-management may be adequate for managing symptoms.[38,39] If symptoms are severe or suicidal intent is present, it is prudent to refer to behavioral health specialists (in primary care if available, specialty care if indicated, or emergency department for crisis).

Behavioral Treatment

The first-line behavioral treatment for anxiety is cognitive-behavioral therapy (CBT), which targets the maladaptive behavioral (eg, avoiding anxiety-provoking situations) and cognitive (eg, interpreting ambiguous situations negatively) patterns that develop and maintain anxiety disorders.[40] CBT is structured and skills focused, comprising psychoeducation and skills training to identify and change maladaptive patterns of thinking and behavior (eg, how to recognize and challenge anxious thoughts).[40]

Meta-analyses of RCTs demonstrate that full-length CBT (typically 10-16 fifty-minute sessions) for anxiety disorders is effective and durable, with meaningful reductions in anxiety symptoms compared to control conditions (eg, wait list, pill placebo, psychological placebo, usual care) maintained over long-term follow-up.[41-43] Brief CBT interventions (6-8 thirty-minute sessions) delivered within primary care by embedded behavioral health consultants are also effective and durable,[44,45] demonstrating equivalent effects to longer-term treatment.[46] Related treatments that are effective in reducing anxiety symptoms include acceptance-based interventions, emphasizing acceptance of emotional experiences in route to pursuing one's values despite symptoms, and mindfulness-based interventions, emphasizing nonjudgmental present-moment awareness.[47,48] Potential downsides of behavioral treatment include limited access to therapists, time commitment, and cost.

Due to visit time constraints and lack of training, most primary care clinicians are unlikely to deliver formal CBT. Rather, they will typically refer patients for brief CBT with embedded behavioral health clinicians if available (see the Integrated Behavioral Health Care subsection) or to specialty mental health clinics. Offering self-help resources based on CBT may also be helpful (Table 2). Digital interventions (eg, internet-delivered psychotherapy) and self-help tools (eg, bibliotherapy), with or without guidance from clinicians, can be effective for reducing anxiety compared to usual care or wait list, particularly for panic disorder, social anxiety disorder, and GAD.[49,50] Mobile applications are a widely accessible self-help tool and have been shown, particularly if based on CBT, to reduce anxiety symptoms compared to inactive controls, placebo, or usual care.[51]

Integrated Behavioral Health Care

We encourage using integrated behavioral health care if available. In the Primary Care Behavioral Health (PCBH) model, an embedded behavioral health consultant delivers focused interventions,[52] typically incorporating techniques from CBT (eg, relaxation training, cognitive restructuring). PCBH is associated with shorter wait times, higher likelihood of engaging in care,[53] and improved mental health outcomes.[54] While patients will vary in how quickly they respond, clinically meaningful improvements in symptoms and functioning have been shown from as few as 1 to 2 PCBH treatment sessions.[55] In the Collaborative Care Management (CoCM) model, primary care clinicians prescribe a psychotropic medication, with consulting psychiatry professionals offering tailored guidance for managing medications, while care managers (eg, registered nurse, social worker) monitor symptoms and provide brief behavioral treatment. CoCM for anxiety disorders has been shown to result in greater reductions in anxiety compared to usual primary care, especially for panic disorder.[56]

Pharmacological Treatment

Anxiety can be treated with daily medications, such as selective serotonin reuptake inhibitors (SSRIs), or short-acting, as-needed medications. Daily medications are best when the anxiety is more frequent, while as-needed, short-acting medications may be appropriate for intermittent symptoms. We focus on GAD, the most common anxiety disorder in primary care[25] and in patients with medical illnesses,[11] as the model for the pharmacological treatment of anxiety disorders.

Treating GAD

In GAD, SSRIs and serotonin-norepinephrine reuptake inhibitors (SNRIs) are first-line treatment options backed by numerous RCTs and meta-analyses.[57-60] The SSRIs and SNRIs with US Food and Drug Administration (FDA) indication to treat GAD are escitalopram, paroxetine, duloxetine, and venlafaxine (**Table 3**). While not FDA-indicated for GAD, meta-analyses of RCTs have also shown other medications, including sertraline and fluoxetine, to be effective.[57] Treatment guidelines of multiple organizations[61-64] suggest first-line treatment with a SSRI or SNRI. These medications tend to be well tolerated without considerable long-term adverse effects. Some potential adverse effects include headache, nausea, insomnia, somnolence, sexual dysfunction, and increased bleeding.[65] When adverse effects occur, they often occur early in the course of treatment, and some of the most common (eg, nausea) tend to improve over several weeks.[66] These medications often take at least 2 weeks to begin to show improvement and up to 3 months for full effect, although benefit in the first 2 to 4 weeks may predict future response.[67]

In considering whether to start an SSRI or SNRI, patient preferences and abilities (eg, desire for medication, time for behavioral therapy) should take precedence. Additional considerations include cost, ease of treatment, and a careful risk-benefit analysis of treatment options. For an adequate trial, it may take several months to reach an optimal dose and see full benefit. Treatment should be

Table 3. Pharmacotherapy Options for Anxiety Disorders[a]

Medication	Medication class	FDA indications for adult anxiety disorders	Starting dose and titration schedule	Contraindications and cautions
Daily medications: typically first-line treatment for anxiety disorders				
Paroxetine	SSRI	GAD, PD, SAD	Immediate release: GAD/SAD: initial, 20 mg daily; increments, 10 mg every 1 wk or longer; maximum, 60 mg daily PD: initial, 10 mg daily; increments, 10 mg every 1 wk or longer; maximum, 60 mg daily Controlled release: SAD: initial, 12.5 mg daily; increments, 12.5 mg every 1 wk or longer; maximum, 37.5 mg daily PD: initial, 12.5 mg daily; increments, 12.5 mg every 1 wk or longer; maximum: 75 mg daily	• More anticholinergic than other SSRIs • On Beers list to avoid use with older adults due to it being highly anticholinergic, sedating, and with risk for orthostatic hypotension • Monitor sodium levels, as SSRIs may exacerbate or cause SIADH or hyponatremia, particularly in older adults • If using in older adults or those with severe kidney or hepatic impairment, start at lower dose (eg, 10 mg daily) and do not exceed 40 mg daily (immediate release) for all indications; 37.5 mg (controlled release) for SAD, and 50 mg (controlled release) for PD • May cause fetal and neonatal harm with an increased risk of congenital malformations when exposed in the first trimester • SSRIs may have increased risk for persistent pulmonary hypertension and withdrawal in newborns when used in the third trimester
Sertraline	SSRI	PD, SAD	PD/SAD: initial, 25 mg daily; increments, 25-50 mg every 1 wk or longer; maximum, 200 mg daily	• Multiple antidepressants, including SSRIs, are on the Beers list to use with caution, and to monitor sodium levels, as they may exacerbate or cause SIADH or hyponatremia, particularly in older adults • Hepatic impairment: • Mild: recommend half dose for starting and maximum dosing • Moderate to severe: not recommended • SSRIs may have increased risk for persistent pulmonary hypertension and withdrawal in newborns when used in the third trimester
Fluoxetine	SSRI	PD	PD/SAD: initial, 10 mg daily; increments, 10 mg every 1 wk or longer; maximum: 60 mg daily	• Use with caution in those with conditions that may predispose to arrythmias, as QT prolongation can occur • Multiple antidepressants, including SSRIs, are on the Beers list to use with caution, and to monitor sodium levels, as they may exacerbate or cause SIADH or hyponatremia, particularly in older adults • Hepatic impairment and older adults: lower or less frequent dosing in those with cirrhosis • SSRIs may have increased risk for persistent pulmonary hypertension and withdrawal in newborns when used in the third trimester
Escitalopram	SSRI	GAD	GAD: initial, 10 mg daily; increments, 5-10 mg every 1 wk or longer; maximum: 20 mg daily	• Multiple antidepressants, including SSRIs, are on the Beers list to use with caution, and to monitor sodium levels, as they may exacerbate or cause SIADH or hyponatremia, particularly in older adults • Hepatic impairment and older adults: recommended dose is 10 mg once daily • SSRIs may have increased risk for persistent pulmonary hypertension and withdrawal in newborns when used in the third trimester
Citalopram	SSRI	None	Off label: initial, 10 mg daily; increments, 10 mg every 1 wk; maximum, 40 mg daily	• Greatest risk of dose-dependent QT prolongation • Multiple antidepressants, including SSRIs, are on the Beers list to use with caution, and to monitor sodium levels, as they may exacerbate or cause SIADH or hyponatremia, particularly in older adults • Older adults, hepatic impairment, and CYP2C19: maximum recommended dose is 20 mg daily • SSRIs may have increased risk for persistent pulmonary hypertension and withdrawal in newborns when used in the third trimester
Fluvoxamine	SSRI	None	Off label: initial, 25-50 mg daily; increments, 25-50 mg every 1 wk or longer; maximum, 300 mg daily Once stabilized on an immediate-release dose, can convert to extended-release once daily dosing; split immediate-release doses >100 mg into twice-daily dosing	• FDA label cautions use with benzodiazepines, particularly diazepam • Multiple antidepressants, including SSRIs, are on the Beers list to use with caution, and to monitor sodium levels, as they may exacerbate or cause SIADH or hyponatremia, particularly in older adults • Hepatic impairment and older adults: may require lower starting and maximum doses and slower titration • SSRIs may have increased risk for persistent pulmonary hypertension and withdrawal in newborns when used in the third trimester

(continued)

Table 3. Pharmacotherapy Options for Anxiety Disorders[a] (continued)

Medication	Medication class	FDA indications for adult anxiety disorders	Starting dose and titration schedule	Contraindications and cautions
Venlafaxine extended release	SNRI	GAD, PD, SAD	GAD/PD: initial, 37.5-75 mg daily; increments, 37.5-75 mg every 1 wk or longer; maximum, 225 mg daily SAD: initial, 75 mg daily; increments, none; maximum, 75 mg daily	• Monitor blood pressure during treatment, as SNRIs can cause elevated blood pressure • Multiple antidepressants, including SNRIs, are on the Beers list to use with caution, and to monitor sodium levels, as they may exacerbate or cause SIADH or hyponatremia, particularly in older adults • Kidney impairment/dialysis: reduce daily dose by 25%-50% in mild impairment, 50% in severe impairment • Hepatic impairment: reduce total dose by 50% in mild to moderate impairment; in severe impairment or cirrhosis, may need to reduce by >50% • SNRIs may have increased risk for persistent pulmonary hypertension and withdrawal in newborns when used in the third trimester
Duloxetine	SNRI	GAD	GAD/PD: initial, 30-60 mg daily; increments, 30-60 mg every 1 wk or longer; maximum, 120 mg daily	• FDA indicated to treat chronic musculoskeletal pain and diabetic peripheral neuropathic pain • Monitor blood pressure during treatment, as SNRIs can cause elevated blood pressure • On Beers list to avoid use with older adults due to increased gastrointestinal adverse effects • Monitor sodium levels, as SNRIs may exacerbate or cause SIADH or hyponatremia, particularly in older adults • Avoid concomitant use with potent inhibitors of CYP1A2 and only use with caution with potent inhibitors of CYP2D6, as both of these may increase duloxetine concentrations • SNRIs may have increased risk for persistent pulmonary hypertension and withdrawal in newborns when used in the third trimester
Other daily medications: in specific cases or when first-line options have failed				
Buspirone	Azapirone	GAD	GAD: initial, 10-15 mg total divided into 2-3 doses (eg, 7.5 mg twice daily); increments, 5 mg every 2-3 d or longer; maximum, 60 mg daily divided into 2-3 doses	• May improve SSRI-induced sexual adverse effects • Kidney impairment: no specific dose adjustments but can have considerably increased concentrations in kidney impairment so would consider lower doses • Hepatic impairment: reduce dose by 50% and slow titration schedule • Consider reducing dose when given with CYP3A4 inhibitors
Mirtazapine	Other antidepressant	None	Off label: initial, 7.5-15 mg daily; increments, 7.5-15 mg every 1 wk or longer; maximum, 60 mg daily	• Can be helpful when insomnia is also present • Monitor kidney and hepatic function, lipids, and weight, as mirtazapine can cause increased appetite, weight gain, and dyslipidemia • Multiple antidepressants, including mirtazapine, are on the Beers list to use with caution, and to monitor sodium levels, as they may exacerbate or cause SIADH or hyponatremia, particularly in older adults • Severe kidney impairment and older adults: start at lower dose and titrate slower • Hepatic impairment: reduce starting and maximum dose by 50%
Short acting or as-needed medications: adjunctive options				
Hydroxyzine	Antihistamine	Anxiety	Initial, 25-50 mg up to 4 times daily; increments, 25 mg every 1 wk or longer; maximum, 100 mg daily up to 4 times daily	• As hydroxyzine can be sedating, daytime doses may need to be lower than what can be tolerated for nighttime doses where sedation may alleviate insomnia from anxiety • On Beers list to avoid use with older adults • Kidney and hepatic impairment: reduce doses to approximately 25%-50% of usual dose based on level of impairment
Propranolol	β-Blocker	None	Off label (performance-only SAD): initial, 10 mg as needed 30-60 min beforehand; increments, 10-20 mg increase as needed; maximum, 60 mg daily	• Used in performance-only SAD; less sedating than other as-needed options • Kidney and hepatic impairment: use with caution, consider reduced dose
Lorazepam	Benzodiazepine	Anxiety	Initial, 0.5-2 mg every 4-6 h as needed; increments, up to 1 mg increase every 2-3 d or longer; maximum, 10 mg total daily dose, although usual maximum is 6 mg daily	• Benzodiazepines may lead to physical and psychological dependence, particularly with higher doses and longer-term use • On Beers list to avoid use with older adults • Avoid use with opioids due to risk of respiratory depression

(continued)

Table 3. Pharmacotherapy Options for Anxiety Disorders[a] (continued)

Medication	Medication class	FDA indications for adult anxiety disorders	Starting dose and titration schedule	Contraindications and cautions
Diazepam	Benzodiazepine	Anxiety	Initial, 2-5 mg 1-2 times daily as needed; increments, up to 1 mg increase every 2-3 d or longer or may increase frequency of dosing gradually up to 4 doses in a day; maximum, 40 mg total daily dose, divided into 2-4 doses	• Benzodiazepines may lead to physical and psychological dependence, particularly with higher doses and longer-term use • On Beers list to avoid use with older adults • Avoid use with opioids due to risk of respiratory depression • Hepatic impairment: half-life can be increased and can contribute to hepatic encephalopathy
Alprazolam	Benzodiazepine	GAD, PD	Anxiety, PD: initial, 0.25-0.5 mg 3 times daily as needed; increments, 0.25-1 mg increase every 3-4 d; maximum, 10 mg total daily dose, although a more common recommended maximum dose is 4-6 mg total	• Benzodiazepines may lead to physical and psychological dependence, particularly with higher doses and longer-term use • On Beers list to avoid use with older adults • Avoid use with opioids due to risk of respiratory depression • Severe hepatic impairment: start at lower dose and titrate more slowly • Contraindicated with ketoconazole and itraconazole; only use with caution with other potent CYP3A inhibitors
Clonazepam	Benzodiazepine	PD	PD: initial, 0.25-0.5 mg 1-2 times daily as needed; increments, 0.25-0.50 mg increase every few days or longer; maximum, 4 mg total daily dose	• Benzodiazepines may lead to physical and psychological dependence, particularly with higher doses and longer-term use • On Beers list to avoid use with older adults • Avoid use with opioids due to risk of respiratory depression
Pregabalin	Anticonvulsant	None	Off label: initial, 150 mg divided into 2-3 doses; increments, up to 150 mg total dose increase weekly but typically 50-100 mg at a time; maximum, 300 mg total daily dose typically, although some data up to 600 mg/d	• Can be helpful in neuropathic pain • Antiepileptic medications, including pregabalin, can increase the risk of suicidal ideation or behavior • On Beers list to avoid use with older adults unless transitioning from opioids • Kidney impairment: reduce starting and maximum dose by 50%-75% in moderate to severe impairment

Abbreviations: FDA, US Food and Drug Administration; GAD, generalized anxiety disorder; PD, panic disorder; SAD, social anxiety disorder; SIADH, syndrome of inappropriate antidiuretic hormone secretion; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

[a] Specific drug information is taken from the FDA label where possible and UpToDate for non-FDA-approved indications. Older adults are defined as those 65 years or older, per 2023 American Geriatrics Society Beers Criteria guidelines.[73]

initiated and then given at least 4 to 6 weeks at a dose to monitor for benefit, while further titration may then be needed for further improvement, with another 4- to 6-week observation period at each dose. In measuring response, serial screenings with the Generalized Anxiety Disorder-7 tool and clinical interview can be helpful in evaluating reduction in anxiety symptoms. We recommend increasing to at least a moderate dose before considering a medication ineffective, unless adverse effects or worsening of symptoms occur. When choosing a starting dose and titration schedule, a balance is required between not delaying symptom improvement and not treating too aggressively in patients who may be more alert or sensitive to adverse effects due to their anxiety. For patients treated with antidepressant medication, discontinuing pharmacotherapy has been associated with a risk of symptom recurrence. Therefore, discontinuing prior to 1 year of treatment may be inadvisable,[68] unless adverse effects or other reasons (eg, cost, drug interactions with other medications) necessitate an earlier discontinuation or switch to an alternate agent.

If first-line treatment is ineffective, a trial of a second SSRI/SNRI is often indicated; the **Figure** illustrates an overall treatment algorithm. The addition of shorter-acting medications such as hydroxyzine or a benzodiazepine can provide earlier symptom relief than SSRIs/SNRIs or serve as a bridge when waiting to access, or realize benefits from, behavioral therapy.[62,63] However, benzodiazepines carry considerable adverse risks, especially with long-term use, so they should only be used for short-term relief and not long-term management of GAD, and only if less risky options such as hydroxyzine have failed.[64] Short-acting medications should be used cautiously for older adults, as many medications (eg, benzodiazepines, hydroxyzine, pregabalin) are not recommended for use in this population (Table 3).[69]

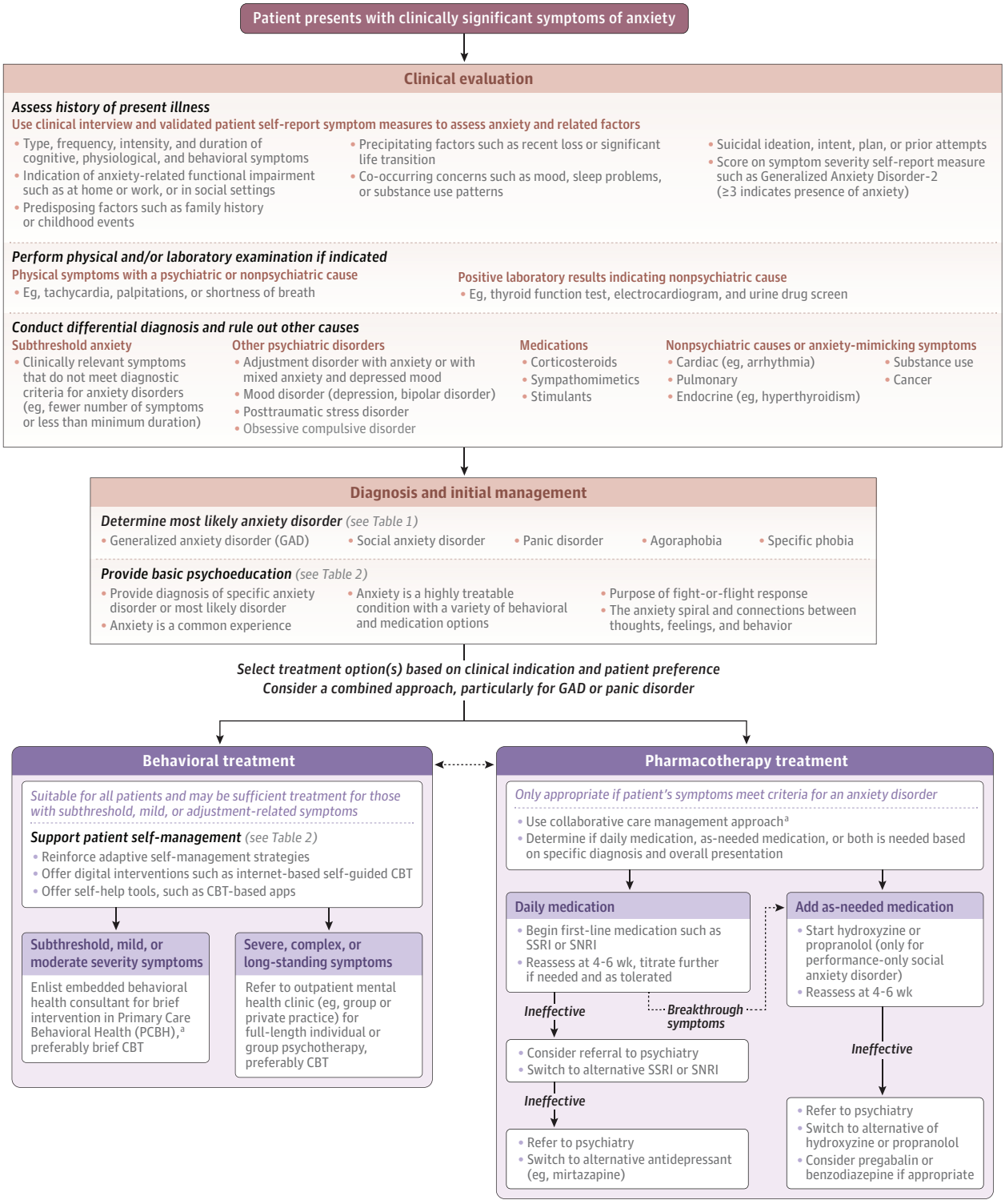
Treating Other Anxiety Disorders

Different approaches may be appropriate for anxiety disorders other than GAD. Table 3 shows FDA-indicated medications for social anxiety, panic disorder, and anxiety disorders broadly. For example, SSRIs and SNRIs are effective in social anxiety, but if the patient is rarely in anxiety-provoking social situations, a daily medication may be more burdensome than an as-needed medication like propranolol or a benzodiazepine. Similarly, panic disorder or a specific phobia tends to be more episodic or triggered, so short-acting options such as hydroxyzine, pregabalin, or propranolol may be effective.[70-72] As-needed, short-acting medications should be considered when symptoms are severe and in need of rapid symptom control or while waiting for a daily medication to take effect.[63,73]

Combined Treatment

Combining behavioral and pharmacological treatment (vs monotherapy) may result in improved outcomes, but the evidence is mixed.[70,74-77] Patient preference, patient characteristics (eg, age), potential adverse effects, and treatment history should be considered, as some evidence sug-

Figure. Flowchart of Anxiety Treatment Options



CBT indicates cognitive-behavioral therapy; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

[a]Integrated behavioral health care resources to utilize if available in the local clinic.

gests combined treatment may be effective for patients who have not responded to monotherapy.[77] The decision to initiate a combined therapy vs monotherapy should consider not only efficacy, but also the time burden required for behavioral therapy, the rapidity of symptom relief, and the durability of effect. The evidence for combined treatment is stronger for the treatment of panic disorder[74-76]

and GAD[76,77] (vs other anxiety disorders) and when antidepressant medication (vs other pharmacotherapies) is combined with behavioral treatment.[70,77]

Prognosis

GAD and social anxiety disorder have a chronic, persistent course if untreated. Only 40% of primary care patients fully recover over 2 to 5 years.[78,79] However, primary care patients with anxiety disorders who received their choice of treatment (CBT, pharmacotherapy, or both) showed response rates (defined as >50% symptom reduction from baseline) of 64% (vs 45% for usual care), with 51% achieving remission by 1 year (vs 33% for usual care).[80] For patients who are not responding when treated in primary care, when symptoms are severe, or when the primary care clinician believes that they need additional specialist support, a referral to psychiatry is indicated for further work-up and treatment.

Limitations

Although we reviewed the literature to integrate the latest evidence, this was not a systematic review. The available evidence has limitations, including that most treatment trials focus on specific disorders[44] and more than half of behavioral treatment trials did not use an active treatment as the comparison condition, instead favoring wait-list controls.[81] We did not include all possible anxiety treatments, such as complementary and alternative medicine approaches or emerging new treatments with limited evidence that are not easily accessible in primary care.

Conclusions

In conclusion, primary care clinicians frequently manage patients with anxiety disorders and symptoms. Effective behavioral and pharmacological treatment options are available and appropriate for primary care settings. Greater implementation of universal screening for anxiety per USPSTF recommendations[16] will help to improve detection, in turn facilitating increased treatment. Clinicians should be mindful of common anxiety presentations and how to efficiently differentiate between anxiety disorders and other psychiatric or medical conditions. Referring patients to behavioral health specialists for brief or full-length CBT and prescribing first-line pharmacotherapy with CoCM can help patients better manage anxiety.

ARTICLE INFORMATION

Accepted for Publication: February 1, 2026.

Published Online: May 4, 2026. doi:10.1001/jamainternmed.2026.0395

Conflict of Interest Disclosures: Dr Shepardson reported grant I01-HX003206 from the US Department of Veterans Affairs/Veterans Health Administration Office of Research and Development, Health Services Research and Development Service. No other disclosures were reported.

Funding/Support: This work was supported by the resources of the VA Center for Integrated Healthcare.

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Disclaimer: These contents do not represent the views of the US Department of Veterans Affairs or the US government.

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