

## VIEWPOINT

# Treating Anxiety in 2017

## Optimizing Care to Improve Outcomes

**Murray B. Stein, MD, MPH**

Department of Psychiatry, University of California San Diego, La Jolla; and VA San Diego Healthcare System, San Diego, California.

**Michelle G. Craske, PhD**

Department of Psychology, University of California-Los Angeles; and Department of Psychiatry and Biobehavioral Sciences, University of California-Los Angeles.

**Anxiety disorders** are prevalent and impairing, and they are a leading cause of disability-adjusted life-years worldwide.<sup>1</sup> The estimated 12-month prevalence of anxiety disorders among US adults is approximately 10%.<sup>2</sup> Yet since 2007, no new anxiolytics have been approved by the US Food and Drug Administration (FDA). Although new anxiety treatments are needed, patients can benefit from existing pharmacological and psychosocial therapies<sup>3</sup> delivered using current best practices.

The most commonly encountered anxiety disorders among patients seen in health care settings include generalized anxiety disorder, panic disorder, social anxiety disorder, and posttraumatic stress disorder (a trauma- and stressor-related disorder in the *DSM-5*). In this Viewpoint, we highlight management considerations for physicians who are not psychiatrists but who treat most patients with anxiety disorders in the United States.

### Evaluation of Anxiety Disorders Can Be Systematically Approached

Features of anxiety disorder include the presence of anxiety (often with physical symptoms such as tachycardia, dyspnea, or gastrointestinal distress), worry, or avoidance that are excessive or out of proportion to the situation, persistent, and associated with impairments in social, occupational, or other important areas of functioning. Whereas full medical diligence, including history (eg, use of caffeine or other stimulants; illicit drug use), physical examination, and other testing (eg, electrocardiogram and measurement of serial troponin level for emergency department patients with chest pain), is indicated for patients presenting with symptoms of anxiety, patients are best served if anxiety disorders are diagnosed (and treated) early after onset. For most patients with new-onset anxiety, a thyroid-stimulating hormone level should be obtained, given the prevalence of thyroid disorders and the ease and safety of testing; other tests such as brain computed tomography, magnetic resonance imaging, electroencephalography, or serial measurements of plasma catecholamine levels usually are not needed. Clinicians can investigate less common diagnostic entities among patients who do not respond to anxiety treatment.

### Most People Function Well Despite Being Stressed

Anxiety disorders may occur with no clear precipitating factors. However, most individuals live stressful lives, and anxiety typically emerges during periods of stress. It is reasonable to watchfully wait and reevaluate the patient's symptoms once the stress has subsided. However, if anxiety persists or regularly recurs during subsequent periods of stress, then an anxiety disorder is likely, and it is time to intervene.

### Measurement of Anxiety Is Important

Treatment of anxiety should be similar to the treatment of blood pressure, in that anxiety should be measured (Figure). But too often, physicians rely on assessments such as "How is your anxiety?" to manage anxiety disorders. By asking patients to complete short (paper-and-pencil, tablet- or smartphone-based) self-report measures at each visit, clinicians can track severity and treatment response. For instance, the Generalized Anxiety Disorder 7-Item Scale (GAD-7)<sup>4</sup> is available at no cost,<sup>5</sup> takes patients 2 to 3 minutes to complete, can be quickly scored by physicians, and is clinically meaningful for other anxiety disorders, not just generalized anxiety disorder. Scores of 5, 10, and 15 correspond to mild, moderate, and severe symptoms, respectively.

### Stepped Care Should Be Stepped Up When Needed

When anxiety treatment is indicated, it is reasonable to start with interventions that are accessible, low-cost, and safe. These include physical exercise and mindfulness-based stress reduction approaches (available through apps or web-based programs). Also, patients should be directed to online sources of high-quality information about their illness and its treatment. Many patients will report some benefit from these approaches, but most will require more than these alone.

### Antidepressants and Cognitive Behavioral Therapies Treat Anxiety Disorders

Mainstay treatments for patients with anxiety include antidepressants (selective serotonin reuptake inhibitors [SSRIs] or serotonin and norepinephrine reuptake inhibitors [SNRIs]) and cognitive behavioral therapies (CBTs).<sup>6</sup> Either treatment modality alone is likely to substantially benefit more than 50% of patients with anxiety. These approaches have been incorporated into collaborative care programs,<sup>7</sup> but their elements can be implemented in most clinical settings. Commonly used SSRIs and SNRIs include duloxetine, escitalopram, fluoxetine, sertraline, and venlafaxine. If pharmacotherapy is chosen, therapy should be initiated with an SSRI or SNRI at the lowest available dose, and the dose should be up-titrated every 2 to 4 weeks to minimize adverse effects while ensuring sufficient time for active effects (Figure). The highest tolerated dose approved by the FDA should be used for at least 2 weeks before the medication is deemed ineffective, at which point switching to a different SSRI or SNRI should be tried.<sup>3</sup> Many patients will discontinue medication at the first sign of an adverse drug effect. The most common adverse effects associated with these drugs include nausea, agitation or sedation, sexual adverse effects (such as decreased libido and delayed orgasm), and, for SNRIs, hypertension. Switching from one medication to

#### Corresponding

**Author:** Murray B. Stein, MD, MPH, Department of Psychiatry, University of California-San Diego, Altman Clinical Research Institute Bldg, 9500 Gilman Dr, MC 0855, La Jolla, CA 92093-0855 (mstein@ucsd.edu).

another without an adequate dose and duration of therapy usually leads to ineffective treatment. Through patient engagement and patience, physicians can ensure that patients receive the therapeutic trials they deserve.

If an antidepressant is effective, it should be continued for 9 to 12 months at therapeutic dose before consideration is given to tapering and stopping. If antidepressants are insufficient for optimizing functioning and reducing distress, the patient should be referred to a suitably trained therapist for CBT (if this option was not chosen initially) or to a psychiatrist for advanced medication management.

### Not All Therapy or Counseling Is CBT

There are many forms of psychological therapy, but the one with the most empirical support for anxiety disorders for all ages is CBT, a goal-oriented short-term therapy designed to reduce overly negative interpretations of situations, replace avoidant behaviors with approach and coping behaviors, and reduce levels of tension and autonomic arousal (Figure). CBT is available through online programs, with good evidence for success when accompanied by some support.<sup>8</sup> A hallmark feature of CBT is assignment of between-session practice (eg, facing situations that have been avoided). An easy way to know if patients have been receiving CBT is to ask what their therapist has asked them to practice.

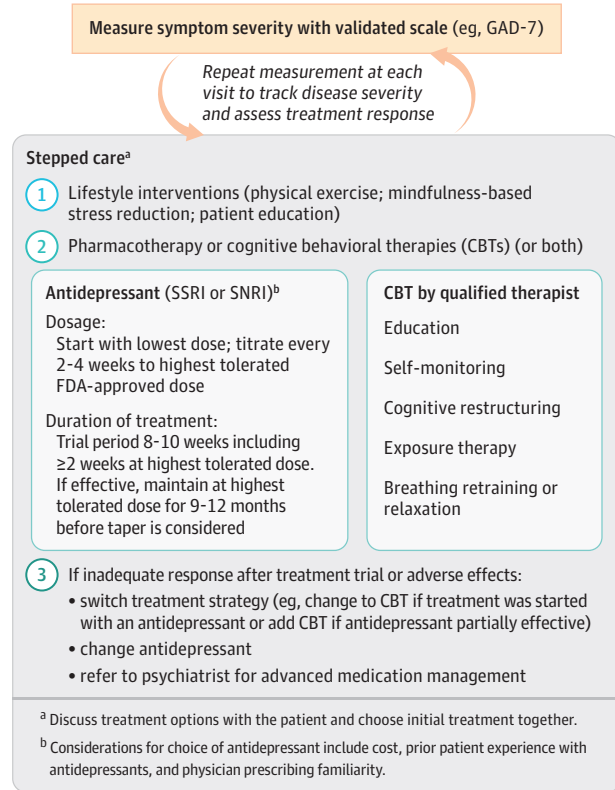
### Benzodiazepines Are to Anxiety What Opioids Are to Pain

When antidepressants are ineffective (or partially effective) and CBT has failed, benzodiazepines can be considered. Like opioids for pain, benzodiazepines for anxiety are highly effective in the short term, liable to be abused by some patients, and generally discouraged but sometimes indispensable for chronic use. Benzodiazepines should be avoided in patients with histories of alcohol or other drug use (gabapentin or pregabalin are potential substitutes). Long-acting benzodiazepines such as clonazepam (taken as scheduled, not as needed) could be considered for treatment-refractory patients.

### Complementary/Alternative and Experimental Therapies Are Just That

Whereas yoga, meditation, and massage confer benefit to some patients with anxiety disorders and are unlikely to do harm, the same cannot be said about experimental treatments such as 3,4-methylenedioxymethamphetamine (MDMA, or "ecstasy") or ketamine. These await further controlled study, and patients should be discouraged from use of these and other unproven approaches

Figure. Treatment of Persistent or Recurrent Anxiety Disorder



FDA indicates US Food and Drug Administration; GAD-7, Generalized Anxiety Disorder 7-Item Scale; SNRI, serotonin and norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

until more is known about efficacy and safety. Cannabis products to treat anxiety have little empirical support and are not recommended.

### Conclusions

Despite the lack of new pharmacological therapies for anxiety in the past decade, the evidence for CBT for anxiety has increased, as has physicians' experience with existing drugs such as SSRIs and SNRIs and a necessary familiarity with the advantages and disadvantages of benzodiazepine use. Although the development of novel therapeutics is expected in the not-too-distant future, effective tools are now available and, when skillfully used, will help improve the lives of patients with anxiety disorders.

#### ARTICLE INFORMATION

**Published Online:** July 5, 2017.  
doi:10.1001/jama.2017.6996

**Conflict of Interest Disclosures:** All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Stein reported receiving consulting fees from Actelion, Dart Neuroscience, Janssen, Neurocrine Biosciences, Pfizer, Resilience Therapeutics, Tonix Pharmaceuticals, and Turing Pharmaceuticals; holding stock options in Oxeia Biopharmaceuticals and Resilience Therapeutics; holding founder shares in Resilience Therapeutics; serving as editor in chief for psychiatry for UpToDate; as editor in chief for *Depression and Anxiety*; and as deputy editor for *Biological Psychiatry*. Dr Craske reported no disclosures.

#### REFERENCES

1. GBD 2015 DALYs and HALE Collaborators. Global, regional, and national disability-adjusted life-years (DALYs) for 315 diseases and injuries and healthy life expectancy (HALE), 1990-2015. *Lancet*. 2016;388(10053):1603-1658.
2. Comer JS, Blanco C, Hasin DS, et al. Health-related quality of life across the anxiety disorders. *J Clin Psychiatry*. 2011;72(1):43-50.
3. Craske MG, Stein MB. Anxiety. *Lancet*. 2016;388(10063):3048-3059.
4. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med*. 2006;166(10):1092-1097.
5. Patient Health Questionnaire (PHQ) Screeners website. <http://www.phqscreeners.com>. Accessed May 11, 2017.
6. Craske MG, Stein MB, Eley TC, et al. Anxiety disorders. *Nat Rev Dis Primers*. 2017;3:17024.
7. Rollman BL, Belnap BH, Mazumdar S, et al. Telephone-delivered stepped collaborative care for treating anxiety in primary care: a randomized controlled trial. *J Gen Intern Med*. 2017;32(3):245-255.
8. Olthuis JV, Watt MC, Bailey K, Hayden JA, Stewart SH. Therapist-supported internet cognitive behavioural therapy for anxiety disorders in adults. *Cochrane Database Syst Rev*. 2016;3:CD011565.