

INTRODUCTION TO ANXIETY DISORDERS AND THEIR PSYCHOPHARMACOLOGY

Dr. Valerie Primeau, MD FRCPC, NOSM Psychiatry Residency Program Curriculum

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SECTION A: INTRODUCTION TO ANXIETY DISORDERS OBJECTIVES

- **Discuss the history of anxiety disorders, evolutionary concepts, classification, anxious traits, and temperaments of anxiety disorders**
- **Describe the neural circuits in fear and anxiety, the cognitive-behavioural concepts, neuropsychology of anxiety disorders, and the psychodynamic concepts of anxiety**
- **Differentiate between normal anxiety and specific anxiety disorders and distinguish the essential features of various types of anxiety disorder according to DSM 5 including specific phobias, social anxiety disorder, panic disorder, agoraphobia, and generalized anxiety disorder**
- **Explain why mood disorders and some anxiety disorders are twice as common in women as men**
- **Find and use commonly used diagnostic and symptom related rating scales for anxiety disorders**

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2014 CANADIAN CLINICAL PRACTICE GUIDELINES FOR THE MANAGEMENT OF ANXIETY, POSTTRAUMATIC STRESS AND OBSESSIVE-COMPULSIVE DISORDERS

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HISTORY OF ANXIETY DISORDERS, EVOLUTIONARY CONCEPTS, CLASSIFICATION, ANXIOUS TRAITS, AND TEMPERAMENTS OF ANXIETY DISORDERS

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1. HISTORY OF ANXIETY DISORDERS

The understanding of anxiety disorders has evolved over centuries. Early conceptualizations, dating back to Hippocrates and Galen, viewed excessive fear or worry as a disturbance of bodily “humours.”

In the 19th and early 20th centuries, clinicians began describing panic, phobias, and generalized worry as discrete conditions.

Sigmund Freud conceptualized anxiety as a signal of unconscious conflict, giving rise to psychodynamic models that dominated until the mid-20th century.

Modern psychiatry, particularly after the publication of DSM-III in 1980, began classifying anxiety disorders as distinct diagnostic entities with operational criteria, paving the way for standardized research and treatment.

Barlow DH. *Anxiety and Its Disorders: The Nature and Treatment of Anxiety and Panic*. 2nd ed. Guilford Press; 2002.

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2. EVOLUTIONARY CONCEPTS

From an evolutionary perspective, anxiety is an adaptive response that enhances survival.

Fear and worry functioned historically to alert individuals to danger, promote vigilance, and facilitate avoidance of harm.

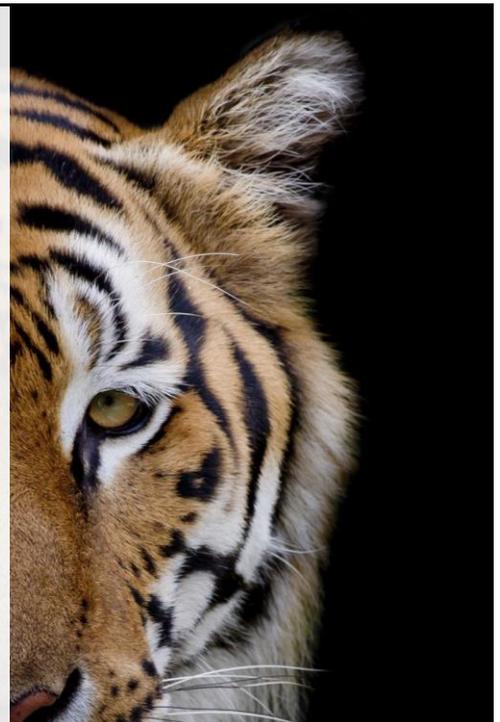
Evolutionary theorists propose that some anxiety disorders represent maladaptive exaggerations of these survival mechanisms.

- For example, excessive social anxiety may have evolved to prevent social exclusion, which historically had life-threatening consequences, while specific phobias may reflect ancestral threats such as snakes, heights, or predatory animals.

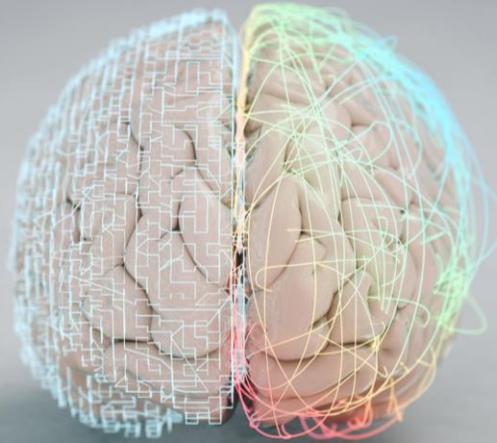
Nesse RM. *Anxiety and the adaptive function of fear*. *Ann NY Acad Sci*. 1990; 60:66–75.

Öhman A, Mineka S. *Fears, phobias, and preparedness: Toward an evolved module of fear and fear learning*. *Psychol Rev*. 2001; 108(3):483–522.

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THE NEURAL CIRCUITS IN FEAR AND ANXIETY, THE COGNITIVE-BEHAVIOURAL CONCEPTS, NEUROPSYCHOLOGY OF ANXIETY DISORDERS, AND THE PSYCHODYNAMIC CONCEPTS OF ANXIETY

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NEURAL CIRCUITS IN FEAR AND ANXIETY

Research has established that the amygdala is central in detecting threat and triggering fear responses.

In healthy functioning, the medial prefrontal cortex regulates amygdala activity and helps suppress fear when it is no longer appropriate.

In anxiety disorders, this regulatory control is often impaired, leading to persistent overactivation of fear responses.

The hippocampus contributes contextual memory, helping the brain distinguish safe from dangerous environments.

Dysfunction in this region contributes to overgeneralization of fear, where anxiety spreads beyond the original threat.

Another key structure, the bed nucleus of the stria terminalis (BNST), is associated with sustained states of anxiety, as opposed to the rapid, phasic fear mediated by the amygdala.

LeDoux JE, Pine DS. Using neuroscience to help understand fear and anxiety: a two-system framework. *Am J Psychiatry*. 2016;173(11):1083–1093.
Bangasser DA, Cuarenta A. Sex differences in anxiety and depression: circuits and mechanisms. *Nat Rev Neurosci*. 2021;22:674–684.

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COGNITIVE-BEHAVIOURAL CONCEPTS OF ANXIETY

Cognitive-behavioural theory conceptualizes anxiety as arising from a combination of distorted thinking patterns and maladaptive behaviours.

Individuals with anxiety often overestimate the likelihood or severity of threat while simultaneously underestimating their ability to cope with these threats.

They frequently engage in catastrophic interpretations of bodily sensations or environmental cues, such as believing that a racing heart signals an impending heart attack or that a minor mistake at work will lead to humiliation.

From a behavioural perspective, anxious individuals engage in avoidance behaviours or safety strategies to reduce immediate distress.

Beck AT, Emery G, Greenberg RL. Anxiety Disorders and Phobias: A Cognitive Perspective. Basic Books; 1985.

Clark DM. A cognitive approach to panic. Behav Res Ther. 1986;24(4):461-470.

Wells A. Meta-cognition and worry: A cognitive model of generalized anxiety disorder. Behav Cogn Psychother. 1995;23(3):301-320.

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COGNITIVE-BEHAVIOURAL AND NEUROPSYCHOLOGICAL CONCEPTS OF ANXIETY



Anxious individuals display attentional biases toward threat: hypervigilance, scanning for danger, and difficulty disengaging once a stimulus is perceived as threatening.



These biases interfere with working memory and executive function, as worry consumes attentional resources.



Avoidance and safety behaviours give short-term relief but reinforce anxiety in the long term.



Together, these patterns create a self-perpetuating cycle of anxiety, sustaining symptoms despite rational recognition of safety.

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COMMON COGNITIVE DISTORTIONS AND ASSUMPTIONS

- **Catastrophizing** – expecting the worst-case scenario.
- **Overestimation of threat** – exaggerating danger.
- **Intolerance of uncertainty** – needing absolute certainty to feel safe.
- **All-or-nothing thinking** – viewing situations in extremes.
- **Selective attention** – focusing only on threat-related cues.
- **Mind reading** – assuming others are judging negatively.
- **Overgeneralization** – drawing broad conclusions from a single event.
- **Safety assumptions** – “If I don’t avoid, something bad will happen.”

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PSYCHODYNAMIC CONCEPTS OF ANXIETY

Psychodynamic theory understands anxiety as a signal of internal conflict.

It arises when unconscious impulses or wishes come into conflict with prohibitions or defenses.

In this framework, symptoms such as avoidance or phobias are seen as defensive strategies that protect the individual from intolerable feelings or conflicts.

Modern psychodynamic approaches also focus on attachment relationships.

Anxiety may reflect unconscious fears of abandonment, loss, or dependency, which are replayed in adult relationships.

Therapy aims to bring these unconscious conflicts into awareness, explore the underlying meanings of symptoms, and help patients develop more adaptive coping mechanisms.

Busch FN, Milrod BL, Singer MB, Aronson A. Psychodynamic Treatment of Panic Disorder: A Guide for Clinicians. American Psychiatric Publishing, 1997.
Shedler J. The efficacy of psychodynamic psychotherapy. Am Psychol. 2010;65(2):98–109.

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NORMAL ANXIETY VS. ANXIETY DISORDERS



Normal Anxiety

- Anxiety is a universal, adaptive response to threat or stress.
- It mobilizes attention, energy, and problem-solving in proportion to the situation (e.g., feeling nervous before an exam).
- It is time-limited and resolves once the stressor passes.
- It does not cause significant impairment in social, occupational, or daily functioning.



Anxiety Disorders

- Anxiety becomes disordered when it is excessive, persistent, and out of proportion to the actual threat.
- Symptoms occur more days than not and often last for months.
- The anxiety leads to avoidance behaviours, distress, and impairment in important areas of life.
- Instead of being protective, the anxiety becomes disabling.

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3. CLASSIFICATION OF ANXIETY DISORDERS

Anxiety disorders are classified in the DSM-5 into several categories, including:

Specific phobias	Social anxiety disorder	Panic disorder	Agoraphobia	Generalized anxiety disorder (GAD)	Separation anxiety disorder	Selective mutism
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Classification allows clinicians and researchers to define diagnostic criteria, guide treatment decisions, and study epidemiology.

These disorders share the hallmark feature of excessive fear or worry, but differ in triggers, duration, and associated behaviours.

OCD and PTSD have been removed from anxiety disorders
 Obsessive-Compulsive and related disorders and their Psychopharmacology
 Trauma- and Stressor- Related Disorders and their Psychopharmacology

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4. ANXIOUS TRAITS AND TEMPERAMENT

Certain traits and temperaments increase susceptibility to anxiety disorders.

Behavioral inhibition, a temperament characterized by wariness in novel situations, is a strong predictor of social anxiety and other anxiety disorders.

High neuroticism, the tendency to experience negative emotions intensely and frequently, is another well-established risk factor.

Additionally, sensitivity to threat and stress reactivity influence how individuals respond to environmental challenges, shaping vulnerability to persistent anxiety.

Understanding these traits helps clinicians identify at-risk populations and tailor preventive or early interventions.

Kagan J. *The Nature of the Child*. Basic Books; 1984.
Barlow DH, Durand VM. *Abnormal Psychology: An Integrative Approach*. 7th ed. Cengage; 2015.

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EPIDEMIOLOGY

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PREVALENCE AND IMPACT

Anxiety and related disorders are among the most common mental disorders, with lifetime prevalence rates as high as 31% and 12-month prevalence rates of about 18%.

Rates for individual disorders vary widely.

Women generally have higher prevalence rates for most anxiety disorders, compared with men.

Anxiety and related disorders are associated with an increased risk of developing a comorbid major depressive disorder.

Unfortunately, anxiety disorders are under-diagnosed and under-treated.

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PREVALENCE AND IMPACT

Anxiety and related disorders put a significant burden on patients and their family members.

They are associated with substantial functional impairment, which increases as the severity of anxiety or the number of comorbid anxiety disorders increases.

In addition, studies have demonstrated quality of life impairments in patients with various anxiety and related disorders.

Anxiety has a considerable economic impact on society as well, being associated with greater use of health care services and decreased work productivity.

Importantly, studies report that about 40% of patients diagnosed with anxiety and related disorder are untreated.

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HYPOTHESES FOR HIGHER FEMALE-TO-MALE PREVALENCE RATIO

Biological Factors

- Hormonal fluctuations (menstrual cycle, pregnancy, menopause) affect serotonin & GABA
- Heightened HPA-axis reactivity → stronger cortisol stress response
- Genetic vulnerabilities interact with female hormonal environment
- Sex differences in fear neurocircuitry (amygdala–prefrontal regulation)

Psychosocial Factors

- Greater exposure to trauma (e.g., sexual assault, IPV)
- Gender roles: unpaid labor, caregiving, chronic stress
- Socioeconomic stressors: poverty, wage gap, single parenting
- Internalizing vs. externalizing coping styles (rumination vs. substance use/aggression)

Diagnostic & Health System Factors

- Women more likely to seek help & report symptoms
- Clinician bias toward diagnosing internalizing disorders in women
- DSM criteria capture internalizing symptoms more readily

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The prevalence difference is not the result of a single cause, but rather an intersection of multiple forces:



Biology sets the stage with hormones, stress reactivity, and genetics.



Society piles on the weight through trauma exposure, social roles, and chronic stressors.



Diagnostics tilt the lens by shaping which symptoms are recognized, reported, and labeled as disorders.



Together, these factors create the observed reality that women are about twice as likely as men to be diagnosed with anxiety and mood disorders.

INTEGRATED UNDERSTANDING

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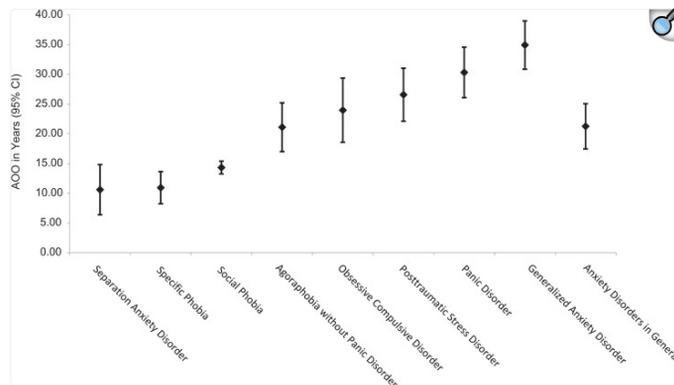
Table 31 Prevalence estimates of anxiety and related disorders among youths in the NCS-A (age 13-18 years)

Anxiety and related disorder	Estimated prevalence (%)	
	12-month	Lifetime
Any anxiety disorder	24.9	31.9
Separation anxiety disorder	1.6	7.6
Specific phobia	15.8	19.3
Social anxiety disorder	8.2	9.1
Posttraumatic stress disorder	3.9	5.0
Panic disorder	1.9	2.3
Generalized anxiety disorder	1.1	2.2

Adapted from references [1155,1156]. NCS-A = National Comorbidity Survey-Adolescent supplement

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Mean age of onset estimates for anxiety disorders. Separation anxiety disorder (SAD; 4 studies; $n = 388$), specific phobia (SP; 11 studies; $n = 7207$), social phobia (SOP; 12 studies; $n = 3407$), agoraphobia without panic disorder (AWP; 8 studies; $n = 1209$), obsessive-compulsive disorder (OCD; 11 studies; $n = 866$), posttraumatic stress disorder (PTSD; 12 studies; $n = 1459$), panic disorder (PD; 11 studies; $n = 3240$), generalized anxiety disorder (GAD; 15 studies; $n = 4422$), and anxiety disorders in general (ANX; 14 studies; $n = 7443$). $I^2 = 93.6\% - 99.7\%$ (all $P < 0.0001$).

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de Lijster, J. M., Dierckx, B., Utens, E. M. W. J., Verhulst, F. C., Zieldorff, C., Dieleman, G. C., & Legerstee, J. S. (2016). The age of onset of anxiety disorders: A meta-analysis. *Psychological Medicine*, 46(12), 2533–2546. <https://doi.org/10.1017/S0033291716000532>

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Lifetime and 12-month Prevalence Rates of Anxiety Disorders Across Gender

Disorder	12-month			Lifetime		
	Women %	Men %	OR [95% CI]	Women %	Men %	OR [95% CI]
PD	4.5	2.2	1.69 [1.29, 2.22] [*]	7.1	4.0	1.70 [1.40, 2.07] [*]
AG	1.9	1.1	ns	3.1	1.7	1.46 [1.07, 1.99] [*]
GAD	4.1	2.1	1.74 [1.37, 2.22] [*]	7.7	4.1	1.83 [1.52, 2.18] [*]
SAD	6.5	4.8	1.24 [1.04, 1.48]	10.3	8.7	ns
Spec	12.0	5.5	2.27 [1.83, 2.81] [*]	16.1	9.0	1.96 [1.63, 2.36] [*]
PTSD	4.3	1.7	2.57 [1.96, 3.36] [*]	8.5	3.4	2.69 [2.18, 3.31] [*]
Any Anxiety	22.7	13.0	1.79 [1.53, 2.10] [*]	33.3	22.0	1.70 [1.48, 1.97] [*]

[Open in a new tab](#)

Note: The table shows odds ratios and 95% confidence intervals in women compared to men; ns: not significant at $p < .05$. Covariates included in the regressions were SES, education level, age, and race.

^{*}significant after a Bonferroni correction of $0.05/20 = 0.0025$. PD = panic disorder; AG = agoraphobia; GAD = generalized anxiety disorder; SAD = social anxiety disorder; Spec = specific phobia; PTSD = post-traumatic stress disorder.

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McLean, C. P., Asnaani, A., Litz, B. T., & Hofmann, S. G. (2011). Gender differences in anxiety disorders: Prevalence, course of illness, comorbidity and burden of illness. *Journal of Psychiatric Research*, 45(8), 1027–1035. <https://doi.org/10.1016/j.jpsychires.2011.03.006>

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SUICIDE RISK

In large surveys, anxiety and related disorders were independently associated with a significant 1.7-2.5 times increased risk of suicide attempts; however, data are conflicting as to whether the risk is moderated by gender.

Increased risk of suicide attempts or completed suicide has been reported for patients with panic disorder, PTSD, and GAD, even in the absence of a comorbid mood disorder.

These data indicate that patients with an anxiety disorder warrant explicit evaluation for suicide risk.

The presence of a comorbid mood disorder significantly increases the risk of suicidal behavior.

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INITIAL ASSESSMENT OF PATIENTS WITH ANXIETY

The management of patients presenting with anxiety symptoms should initially follow the flow of the five main components outlined in Table 3.

Table 3 Overview of the management of anxiety and related disorders

- Screen for anxiety and related symptoms
- Conduct differential diagnosis (consider severity, impairment, and comorbidity)
- Identify specific anxiety or related disorder
- Psychological and/or pharmacological treatment
- Perform follow-up

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Anxiety and related disorders are generally characterized by the features of excessive anxiety, fear, worry, and avoidance.



While anxiety can be a normal part of everyday life, anxiety disorders are associated with functional impairment; as part of the key diagnostic criteria for anxiety disorders is the requirement that the symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning



Asking patients if they are feeling nervous, anxious or on edge, or whether they have uncontrollable worry, can be useful to detect anxiety in patients in whom the clinician suspects an anxiety or related disorder

SCREEN FOR ANXIETY AND RELATED SYMPTOMS

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SCREEN FOR ANXIETY AND RELATED SYMPTOMS

The DSM-5 suggests the questions shown in Table 4 for the identification of anxiety-related symptoms; items scored as mild or greater may warrant further assessment.

If anxiety symptoms are endorsed, they should be explored in more detail by including questions about the onset of the anxiety symptoms, associations with life events or trauma, the nature of the anxiety, and the impact they have had on the patient's current functioning.

Table 4 General screening questions

- During the past two weeks how much have you been bothered by the following problems?
 - Feeling nervous, anxious, frightened, worried, or on edge
 - Feeling panic or being frightened
 - Avoiding situations that make you anxious

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SCREEN FOR ANXIETY AND RELATED SYMPTOMS

Table 5 presents suggested screening questions for individual anxiety and related disorders, from various validated screening tools

Table 5 Screening questions for specific anxiety and related disorders

Panic disorder – MACSCREEN [29,30]

- Do you have sudden episodes/spells/attacks of intense fear or discomfort that are unexpected or out of the blue?

If you answered "YES" then continue

- Have you had more than one of these attacks?
- Does the worst part of these attacks usually peak within several minutes?
- Have you ever had one of these attacks and spent the next month or more living in fear of having another attack or worrying about the consequences of the attack?

SAD (Based on Mini-SPIN [28])

- Does fear of embarrassment cause you to avoid doing things or speaking to people?
- Do you avoid activities in which you are the center of attention?
- Is being embarrassed or looking stupid among your worst fears?

GAD [31]

- During the past 4 weeks, have you been bothered by feeling worried, tense, or anxious most of the time?
- Are you frequently tense, irritable, and having trouble sleeping?

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Table 8 Key features of specific anxiety and related disorders

Disorder	Key features
Panic disorder	<ul style="list-style-type: none"> • Recurrent unexpected panic attacks, in the absence of triggers • Persistent concern about additional panic attacks and/or maladaptive change in behavior related to the attacks
Agoraphobia	<ul style="list-style-type: none"> • Marked, unreasonable fear or anxiety about a situation • Active avoidance of feared situation due to thoughts that escape might be difficult or help unavailable if panic-like symptoms occur
Specific phobia	<ul style="list-style-type: none"> • Marked, unreasonable fear or anxiety about a specific object or situation, which is actively avoided (e.g., flying, heights, animals, receiving an injection, seeing blood)
Social anxiety disorder (SAD)	<ul style="list-style-type: none"> • Marked, excessive or unrealistic fear or anxiety about social situations in which there is possible exposure to scrutiny by others • Active avoidance of feared situation
Generalized anxiety disorder (GAD)	<ul style="list-style-type: none"> • Excessive, difficult to control anxiety and worry (apprehensive expectation) about multiple events or activities (e.g., school/work difficulties) • Accompanied by symptoms such as restlessness/feeling on edge or muscle tension

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General Anxiety / GAD

- **GAD-7 (Generalized Anxiety Disorder-7)** – 7-item self-report scale; measures severity and tracks change over time.
- **Hamilton Anxiety Rating Scale (HAM-A)** – Clinician-administered; widely used in trials and clinical monitoring.
- **Zung Self-Rating Anxiety Scale (SAS)** – 20-item self-report scale; assesses the level of anxiety in adults and helps track treatment progress.
- **Anxiety Symptoms Questionnaire (ASQ)** – Self-report measure; evaluates a broad range of anxiety symptoms and can be used to monitor symptom changes over time.

Panic Disorder

- **Panic Disorder Severity Scale (PDSS)** – Clinician-administered; measures panic frequency, distress, and avoidance.
- **Sheehan Panic Disorder Scale** – Sometimes used as a patient-reported version.

Social Anxiety Disorder

- **Liebowitz Social Anxiety Scale (LSAS)** – Clinician-administered or self-report; assesses fear and avoidance in social situations.

SCALES

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GAD-7 (GENERALIZED ANXIETY DISORDER-7)

GAD-7 Anxiety

Over the last two weeks, how often have you been bothered by the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious, or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid, as if something awful might happen	0	1	2	3

Column totals ___ + ___ + ___ + ___ =
Total score ___

If you checked any problems, how difficult have they made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all Somewhat difficult Very difficult Extremely difficult

Source: Primary Care Evaluation of Mental Disorders Patient Health Questionnaire (PRIME-MD-PHQ). The PHQ was developed by Drs. Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke, and colleagues. For research information, contact Dr. Spitzer at rls@columbia.edu. PRIME-MD® is a trademark of Pfizer Inc. Copyright© 1999 Pfizer Inc. All rights reserved. Reproduced with permission.

Scoring GAD-7 Anxiety Severity

This is calculated by assigning scores of 0, 1, 2, and 3 to the response categories, respectively, of "not at all," "several days," "more than half the days," and "nearly every day." GAD-7 total score for the seven items ranges from 0 to 21.

- 0-4: minimal anxiety
 - 5-9: mild anxiety
 - 10-14: moderate anxiety
 - 15-21: severe anxiety
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HAMILTON ANXIETY RATING SCALE (HAM-A)

Hamilton Anxiety Rating Scale (HAM-A)

Below is a list of phrases that describe certain feeling that people have. Rate the patients by finding the answer which best describes the extent to which he/she has these conditions. Select one of the five responses for each of the fourteen questions.

0 = Not present, 1 = Mild, 2 = Moderate, 3 = Severe, 4 = Very severe.

- | | |
|--|--|
| <p>1 Anxious mood 0 1 2 3 4</p> <p>Worries, anticipation of the worst, fearful anticipation, irritability.</p> | <p>8 Somatic (sensory) 0 1 2 3 4</p> <p>Tinnitus, blurring of vision, hot and cold flushes, feelings of weakness, pricking sensation.</p> |
| <p>2 Tension 0 1 2 3 4</p> <p>Feelings of tension, fatigability, startle response, moved to tears easily, trembling, feelings of restlessness, inability to relax.</p> | <p>9 Cardiovascular symptoms 0 1 2 3 4</p> <p>Tachycardia, palpitations, pain in chest, throbbing of vessels, fainting feelings, missing beat.</p> |
| <p>3 Fears 0 1 2 3 4</p> <p>Of dark, of strangers, of being left alone, of animals, of traffic, of crowds.</p> | <p>10 Respiratory symptoms 0 1 2 3 4</p> <p>Pressure or constriction in chest, choking feelings, sighing, dyspnea.</p> |
| <p>4 Insomnia 0 1 2 3 4</p> <p>Difficulty in falling asleep, broken sleep, unsatisfying sleep and fatigue on waking, dreams, nightmares, night terrors.</p> | <p>11 Gastrointestinal symptoms 0 1 2 3 4</p> <p>Difficulty in swallowing, wind abdominal pain, burning sensations, abdominal fullness, nausea, vomiting, borborygmi, looseness of bowels, loss of weight, constipation.</p> |
| <p>5 Intellectual 0 1 2 3 4</p> <p>Difficulty in concentration, poor memory.</p> | <p>12 Genitourinary symptoms 0 1 2 3 4</p> <p>Frequency of micturition, urgency of micturition, amenorrhea, menorrhagia, development of frigidity, premature ejaculation, loss of libido, impotence.</p> |
| <p>6 Depressed mood 0 1 2 3 4</p> <p>Loss of interest, lack of pleasure in hobbies, depression, early waking, diurnal swing.</p> | <p>13 Autonomic symptoms 0 1 2 3 4</p> <p>Dry mouth, flushing, pallor, tendency to sweat, giddiness, tension headache, raising of hair.</p> |
| <p>7 Somatic (muscular) 0 1 2 3 4</p> <p>Pains and aches, twitching, stiffness, myoclonic jerks, grinding of teeth, unsteady voice, increased muscular tone.</p> | <p>14 Behavior at interview 0 1 2 3 4</p> <p>Fidgeting, restlessness or pacing, tremor of hands, furrowed brow, strained face, sighing or rapid respiration, facial pallor, swallowing.</p> |

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ANXIETY SYMPTOMS QUESTIONNAIRE (ASQ)

Appendix
ANXIETY SYMPTOMS QUESTIONNAIRE (ASQ)

Please read each item and fill each box with the number in the scales below that best describes your experience regarding the Intensity (A) and Frequency (B) of these symptoms:

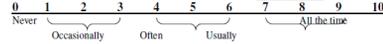
A. USE THIS SCALE TO COMPLETE COLUMN (A) BELOW

How INTENSE or BOTHERSOME the symptom(s) have been in the past week, using the following scale:



B. USE THIS SCALE TO COMPLETE COLUMN (B) BELOW

How FREQUENTLY have you experienced the symptom(s) in the past week, using the following scale:



IN THE PAST WEEK:	A INTENSITY (0 to 10)	B FREQUENCY (0 to 10)
1. Anxiety		
2. Nervousness		
3. Worrying		
4. Irritability		
5. Muscle Tension or Tightness		
6. Trouble Relaxing		
7. Trouble Falling or Staying Asleep <i>(Rate the most troublesome symptom)</i>		
8. Fatigue or Lack of Energy		

9. Problems with Concentration or Attention		
10. Trouble Remembering Things		
11. Shortness of Breath, Chest Tightness or Pain, Pounding/Skipping/Racing Heartbeat <i>(Rate the most troublesome symptom)</i>		
12. Stomach Upset, Nausea, Constipation, Diarrhea, or Irritable Bowels <i>(Rate the most troublesome symptom)</i>		
13. Dizziness, Lightheadedness, Headaches, Trembling or Shakiness <i>(Rate the most troublesome symptom)</i>		
14. Numbness, Tingling, Excessive Sweating, Flushing or Frequent Urination <i>(Rate the most troublesome symptom)</i>		
15. Feeling Restless, Keyed Up, or On Edge		
16. Anticipating or Fearing Something Bad Might Happen		
17. Trouble Functioning at Home, Work, or Socially <i>(Rate the most troublesome symptom)</i>		

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ZUNG SELF-RATING ANXIETY SCALE (SAS)

Zung Self-Rating Anxiety Scale (SAS)

For each item below, please place a check mark (✓) in the column which best describes how often you felt or behaved this way during the past several days. Bring the completed form with you to the office for scoring and assessment during your office visit.

Place check mark (✓) in correct column.	A little of the time	Some of the time	Good part of the time	Most of the time
1 I feel more nervous and anxious than usual.				
2 I feel afraid for no reason at all.				
3 I get upset easily or feel panicky.				
4 I feel like I'm falling apart and going to pieces.				
5 I feel that everything is all right and nothing bad will happen.				
6 My arms and legs shake and tremble.				
7 I am bothered by headaches neck and back pain.				
8 I feel weak and get tired easily.				
9 I feel calm and can sit still easily.				
10 I can feel my heart beating fast.				
11 I am bothered by dizzy spells.				
12 I have fainting spells or feel like it.				
13 I can breathe in and out easily.				
14 I get feelings of numbness and tingling in my fingers & toes.				
15 I am bothered by stomach aches or indigestion.				
16 I have to empty my bladder often.				
17 My hands are usually dry and warm.				
18 My face gets hot and blushes.				
19 I fall asleep easily and get a good night's rest.				
20 I have nightmares.				

Source: William W.K. Zung. A rating instrument for anxiety disorders. Psychosomatics, 1971

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Panic Disorder Severity Scale (PDSS)

**PANIC
DISORDER
SEVERITY
SCALE (PDSS)**

Instructions:

Several of the following questions refer to panic attacks and limited symptom attacks. For this questionnaire we define a panic attack as a sudden rush of fear or discomfort accompanied by at least 4 of the symptoms listed below. In order to qualify as a sudden rush, the symptoms must peak within 10 minutes. Episodes like panic attacks but having fewer than 4 of the listed symptoms are called limited symptom attacks. Here are the symptoms to count:

Rapid or pounding heartbeat, Chest pain or discomfort, Chills or hot flushes, Sweating, Nausea, Trembling or shaking, Dizziness or faintness, Fear of losing control or going crazy, Breathlessness, Feelings of unreality, Fear of dying, Feeling of choking, Numbness or tingling.

1	How many panic and limited symptoms attacks did you have during the week?
0	No panic or limited symptom episodes
1	Mild: no full panic attacks and no more than 1 limited symptom attack/day
2	Moderate: 1 or 2 full panic attacks and/or multiple limited symptom attacks/day
3	Severe: more than 2 full attacks but not more than 1/day on average
4	Extreme: full panic attacks occurred more than once a day, more days than not
2	If you had any panic attacks during the past week, how distressing (uncomfortable, frightening) were they while they were happening? (If you had more than one, give an average rating. If you didn't have any panic attacks but did have limited symptom attacks, answer for the limited symptom attacks.)
0	Not at all distressing, or no panic or limited symptom attacks during the past week
1	Mildly distressing (not too intense)
2	Moderately distressing (intense, but still manageable)
3	Severely distressing (very intense)
4	Extremely distressing (extreme distress during all attacks)
3	During the past week, how much have you worried or felt anxious about when your next panic attack would occur or about fears related to the attacks (for example, that they could mean you have physical or mental health problems or could cause you social embarrassment)?
0	Not at all
1	Occasionally or only mildly
2	Frequently or moderately
3	Very often or to a very disturbing degree
4	Nearly constantly and to a disabling extent

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**PANIC
DISORDER
SEVERITY
SCALE (PDSS)**

4 During the past week were there any places or situations (e.g., public transportation, movie theaters, crowds, bridges, tunnels, shopping malls, being alone) you avoided, or felt afraid of (uncomfortable in, wanted to avoid or leave), because of fear of having a panic attack? Are there any other situations that you would have avoided or been afraid of if they had come up during the week, for the same reason? If yes to either question, please rate your level of fear and avoidance this past week.

- 0 None: no fear or avoidance
- 1 Mild: occasional fear and/or avoidance but I could usually confront or endure the situation. There was little or no modification of my lifestyle due to this
- 2 Moderate: noticeable fear and/or avoidance but still manageable. I avoided some situations, but I could confront them with a companion. There was some modification of my lifestyle because of this, but my overall functioning was not impaired
- 3 Severe: extensive avoidance. Substantial modification of my lifestyle was required to accommodate the avoidance making it difficult to manage usual activities
- 4 Extreme: pervasive disabling fear and/or avoidance. Extensive modification in my lifestyle was required such that important tasks were not performed

5 During the past week, were there any activities (e.g., physical exertion, sexual relations, taking a hot shower or bath, drinking coffee, watching an exciting or scary movie) that you avoided, or felt afraid of (uncomfortable doing, wanted to avoid or stop), because they caused physical sensations like those you feel during panic attacks or that you were afraid might trigger a panic attack? Are there any other activities that you would have avoided or been afraid of if they had come up during the week for that reason? If yes to either question, please rate your level of fear and avoidance of those activities this past week.

- 0 No fear or avoidance of situations or activities because of distressing physical sensations
- 1 Mild: occasional fear and/or avoidance, but usually I could confront or endure with little distress activities that cause physical sensations. There was little modification of my lifestyle due to this
- 2 Moderate: noticeable avoidance but still manageable. There was definite, but limited, modification of my lifestyle such that my overall functioning was not impaired
- 3 Severe: extensive avoidance. There was substantial modification of my lifestyle or interference in my functioning
- 4 Extreme: pervasive and disabling avoidance. There was extensive modification in my lifestyle due to this such that important tasks or activities were not performed

6 During the past week, how much did the above symptoms altogether (panic and limited symptom attacks, worry about attacks, and fear of situations and activities because of attacks) interfere with your ability to work or carry out your responsibilities at home? (If your work or home responsibilities were less than usual this past week, answer how you think you would have done if the responsibilities had been usual.)

- 0 No interference with work or home responsibilities
- 1 Slight interference with work or home responsibilities, but I could do nearly everything I could if I didn't have these problems
- 2 Significant interference with work or home responsibilities, but I still could manage to do the things I needed to do
- 3 Substantial impairment in work or home responsibilities; there were many important things I couldn't do because of these problems
- 4 Extreme, incapacitating impairment such that I was essentially unable to manage any work or home responsibilities

7 During the past week, how much did panic and limited symptom attacks, worry about attacks and fear of situations and activities because of attacks interfere with your social life? (If you didn't have many opportunities to socialize this past week, answer how you think you would have done if you did have opportunities.)

- 0 No interference
- 1 Slight interference with social activities, but I could do nearly everything I could if I didn't have these problems.
- 2 Significant interference with social activities but I could manage to do most things if I made the effort
- 3 Substantial impairment in social activities; there are many social things I couldn't do because of these problems
- 4 Extreme, incapacitating impairment, such that there was hardly anything social I could do

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SHEEHAN PANIC DISORDER SCALE

Sheehan Patient-Rated Anxiety Scale

Features

- Patient administered
- Identifies and measures severity of symptoms associated with anxiety

Scoring and interpretation
Assign a value of 0 to the first answer column ("Not at all"), 1 to the second column, 2 to the third, and so on. Scores above 30 are usually considered abnormal, and scores above 80 are severe. The mean score in panic disorder and agoraphobia is 37 ± 20. The goal of treatment is to bring the score below 10.

	0	1	2	3	4
1 Difficulty in getting your breath, smothering, or overbreathing.					
2 Choking sensation or lump in throat.					
3 Skipping, racing, or pounding of your heart.					
4 Chest pain, pressure, or discomfort.					
5 Bouts of excessive sweating.					
6 Faintness, light-headedness, or dizzy spells.					
7 Sensation of rubbery or "jelly" legs.					
8 Feeling off balance or unsteady like you might fall.					
9 Nausea or stomach problems.					
10 Feeling that things around you are strange, unreal, foggy, or detached from you.					
11 Feeling outside or detached from part or all of your body, or a floating feeling.					
12 Tingling or numbness in parts of your body.					
13 Hot flashes or cold chills.					
14 Shaking or trembling.					
15 Having a fear that you are dying or that something terrible is about to happen.					
16 Feeling you are losing control or going insane.					
17 Sudden anxiety attacks with three or more of the symptoms (listed above) that occur when you are in or about to go into a situation that is likely, from your experience, to bring on an attack.					
18 Sudden unexpected anxiety attacks with three or more symptoms (listed above) that occur with little or no provocation (ie, when you are not in a situation that is likely, from your experience, to bring on an attack).					

Adapted with permission of Sheehan DV From Medicine 73, Metzlaff RL, eds. *Diagnosis and Treatment of Anxiety Disorders: A Physician's Handbook*. Washington, DC: American Psychiatric Press Inc; 1989:98-99.

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SHEEHAN PANIC DISORDER SCALE

	0	1	2	3	4
19 Sudden unexpected spells with only one or two symptoms (listed above) that occur with little or no provocation (ie, when you are not in a situation that is likely, from your experience, to bring on an attack).					
20 Anxiety episodes that build up as you anticipate doing something that is likely, from your experience, to bring on anxiety that is more intense than most people experience in such situations.					
21 Avoiding situations because they frighten you.					
22 Being dependent on others.					
23 Tension and inability to relax.					
24 Anxiety, nervousness, restlessness.					
25 Spells of increased sensitivity to sound, light, or touch.					
26 Attacks of diarrhea.					
27 Worrying about your health too much.					
28 Feeling tired, weak, and exhausted easily.					
29 Headaches or pains in neck or head.					
30 Difficulty in falling asleep.					
31 Waking in the middle of the night or restless sleep.					
32 Unexpected waves of depression occurring with little or no provocation.					
33 Emotions and moods going up and down a lot in response to changes around you.					
34 Recurrent and persistent ideas, thoughts, impulses, or images that are intrusive, unwanted, senseless, or repugnant.					
35 Having to repeat the same action in a ritual, eg, checking, washing, counting repeatedly, when it's not really necessary.					

Patient name _____ Date _____

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Liebowitz Social Anxiety Scale Liebowitz MR. Social Phobia. Mod Probl Pharmacopsychiatry 1987;22:141-173

Pt Name: _____ Pt ID #: _____
 Date: _____ Clinic #: _____ Assessment point: _____

Fear or Anxiety:
 0 = None
 1 = Mild
 2 = Moderate
 3 = Severe

Avoidance:
 0 = Never (0%)
 1 = Occasionally (1—33%)
 2 = Often (33—67%)
 3 = Usually (67—100%)

LIEBOWITZ SOCIAL ANXIETY SCALE (LSAS)

	Fear or Anxiety	Avoidance	
1. Telephoning in public. (P)			1.
2. Participating in small groups. (P)			2.
3. Eating in public places. (P)			3.
4. Drinking with others in public places. (P)			4.
5. Talking to people in authority. (S)			5.
6. Acting, performing or giving a talk in front of an audience. (P)			6.
7. Going to a party. (S)			7.
8. Working while being observed. (P)			8.
9. Writing while being observed. (P)			9.
10. Calling someone you don't know very well. (S)			10.
11. Talking with people you don't know very well. (S)			11.
12. Meeting strangers. (S)			12.
13. Urinating in a public bathroom. (P)			13.
14. Entering a room when others are already seated. (P)			14.
15. Being the center of attention. (S)			15.
16. Speaking up at a meeting. (P)			16.
17. Taking a test. (P)			17.
18. Expressing a disagreement or disapproval to people you don't know very well. (S)			18.
19. Looking at people you don't know very well in the eyes. (S)			19.
20. Giving a report to a group. (P)			20.
21. Trying to pick up someone. (P)			21.
22. Returning goods to a store. (S)			22.
23. Giving a party. (S)			23.
24. Resisting a high pressure salesperson. (S)			24.

DSM-5 CRITERIA REVIEW

Table 19 DSM-5 diagnosis of SAD (social phobia)

- Marked fear or anxiety about social situations in which the person may be exposed to scrutiny by others
- Fear that actions or showing anxiety symptoms will cause negative evaluation (e.g., embarrassment, humiliation) or offend others
- The social situation:
 - Almost always provokes fear or anxiety
 - Is actively avoided or endured with marked fear or anxiety
- The fear, anxiety, or avoidance:
 - Is out of proportion to the actual threat posed by the social situation
 - Is persistent, typically ≥ 6 months
 - Causes significant distress or functional impairment
- If another medical condition is present (e.g., stuttering, obesity), the disturbance is unrelated or out of proportion to it
- Specify “performance only” if the fear is restricted to speaking or performing in public

Adapted from DSM-5 [26].

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Table 11 DSM-5 criteria for panic attacks

- An abrupt surge of intense fear or intense discomfort that reaches a peak within minutes, and includes ≥ 4 of the following symptoms:
 - (1) Palpitations, pounding heart, or accelerated heart rate
 - (2) Sweating
 - (3) Trembling or shaking
 - (4) Sensations of shortness of breath or smothering
 - (5) Feelings of choking
 - (6) Chest pain or discomfort
 - (7) Nausea or abdominal distress
 - (8) Feeling dizzy, unsteady, light-headed, or faint
 - (9) Chills or heat sensations
 - (10) Paresthesias (numbness or tingling sensations)
 - (11) Derealization (feelings of unreality) or depersonalization (being detached from oneself)
 - (12) Fear of losing control or going crazy
 - (13) Fear of dying

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Table 12 DSM-5 diagnosis of panic disorder

- The person has experienced both of the following:
 - Recurrent unexpected panic attacks
 - ≥ 1 of the attacks followed by ≥ 1 month of 1 or both of the following:
 - Persistent concern or worry about additional panic attacks or their consequences
 - Significant maladaptive change in behavior related to the attacks
-

Adapted from DSM-5 [26].

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Table 13 DSM-5 diagnosis of agoraphobia

- Marked fear or anxiety about ≥ 2 of the following 5 groups of situations:
 - (1) Public transportation (e.g., traveling in automobiles, buses, trains, ships, or planes)
 - (2) Open spaces (e.g., parking lots, market places, or bridges)
 - (3) Being in shops, theatres, or cinemas
 - (4) Standing in line or being in a crowd
 - (5) Being outside of the home alone in other situations
 - The individual fears or avoids these situations due to thoughts that escape might be difficult or help might not be available in the event of panic-like symptoms
 - The agoraphobic situations almost always provoke fear or anxiety
 - The situations are actively avoided, require presence of a companion, or endured with marked fear or anxiety
 - The fear or anxiety is out of proportion to actual danger posed by agoraphobic situation
 - The fear, anxiety, or avoidance is persistent, typically lasting ≥ 6 months
 - The fear, anxiety, and avoidance cause clinically significant distress or functional impairment
-

Adapted from DSM-5 [26].

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Table 16 DSM-5 diagnosis of specific phobia

- Marked fear or anxiety about a specific object or situation (e.g., flying, seeing blood)
- The phobic object or situation almost always provokes immediate fear or anxiety and is actively avoided or endured with marked fear or anxiety
- The fear or anxiety is out of proportion to the actual danger posed by the specific object or situation
- The fear, anxiety, or avoidance is persistent, typically ≥ 6 months
- There is marked distress or functional impairment

Adapted from DSM-5 [26].

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Table 17 Specific phobia specifiers in DSM-5

Specifier	Examples
Animal	Spiders, insects, dogs
Natural environment	Heights, storms, water
Blood-injection-injury	Needles, invasive medical procedures
Situational	Airplanes, elevators, enclosed spaces
Other	Choking or vomiting. In children, loud sounds or costumed characters

Adapted from DSM-5 [26].

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Table 22 DSM-5 diagnosis of GAD

- Excessive anxiety and worry (apprehensive expectation) about a number of events or activities (e.g., school/work performance)
- The individual finds it difficult to control the worry
- Excessive anxiety and worry are associated with ≥ 3 of the following symptoms (with at least some occurring more days than not for ≥ 6 months):
 - Restlessness or feeling keyed-up or on edge, being easily fatigued, difficulty concentrating, irritability, muscle tension, or sleep disturbance
- The disturbance causes clinically significant distress or functional impairment

Adapted from DSM-5 [26].

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Table 32 DSM-5 diagnostic criteria for anxiety and related disorders specific to children

Anxiety or related disorder	DSM-5 diagnoses specific to children
Separation anxiety disorder	<ul style="list-style-type: none"> • Developmentally inappropriate and excessive fear or anxiety concerning separation from those to whom the individual is attached, as evidenced by ≥ 3 of the following: <ul style="list-style-type: none"> ◦ Distress when separation occurs, worry about loss or separation, reluctance to leave home, be alone, or go to sleep because of fear of separation, nightmares involving separation, or complaints of physical symptoms (e.g., headaches, upset stomach) when separation occurs • Duration of at least 4 weeks • Onset before 18 years of age • The disturbance causes clinically significant distress or impairment in social, academic (occupational), or other important areas of functioning
Selective mutism	<ul style="list-style-type: none"> • Consistent failure to speak in specific social situations in which there is an expectation for speaking (e.g., at school) despite speaking in other situations
Anxiety or related disorder	Changes to adult DSM-5 diagnostic criteria specific to children
Specific phobia	<ul style="list-style-type: none"> • The fear or anxiety may be expressed by crying, tantrums, freezing, or clinging • Other specifiers: loud sounds or costumed characters
SAD (social phobia)	<ul style="list-style-type: none"> • The anxiety must occur in peer settings, not just during interactions with adults • The fear or anxiety may be expressed by crying, tantrums, freezing, clinging, shrinking, or failure to speak in social situations
OCD, panic disorder	<ul style="list-style-type: none"> • No pediatric specific criteria
PTSD	<ul style="list-style-type: none"> • Qualifiers in children <ul style="list-style-type: none"> ◦ Intrusion symptoms: repetitive play may occur in which themes or aspects of the traumatic event(s) are expressed; there may be frightening dreams without recognizable content; trauma-specific re-enactment may occur in play • Specific subtype for children ≤ 6 years of age
GAD	<ul style="list-style-type: none"> • Less stringent criteria for symptoms than in adults

Adapted from DSM-5 [26].

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CONDUCT DIFFERENTIAL DIAGNOSIS

The differential diagnosis of anxiety and related disorders should consider whether the anxiety is due to another medical or psychiatric condition, is comorbid with another medical or psychiatric condition, or is medication-induced or drug-related.

When a patient presents with excessive or uncontrollable anxiety it is important to identify other potential causes of the symptoms, including direct effects of a substance (e.g., drug abuse or medication) or medical condition (e.g., hyperthyroidism, cardiopulmonary disorders, traumatic brain injury), or another mental disorder.

However, since comorbid conditions are common, the presence of some of these other conditions may not preclude the diagnosis of an anxiety or related disorder.

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RISK FACTORS

Certain risk factors have been associated with anxiety and related disorders and should increase the clinician's index of suspicion (Table 6).

A family or personal history of mood or anxiety disorders is an important predictor of anxiety symptoms.

In addition, family history is associated with a more recurrent course, greater impairment, and greater service use.

A personal history of stressful life events is also associated the development of anxiety and related disorders, in particular, childhood abuse.

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RISK FACTORS

Women generally have higher prevalence rates across all anxiety and related disorders, compared with men.

The median of age of onset is very early for some phobias and for separation anxiety disorder (seven to 14 years), but later for GAD, panic disorder, and PTSD (24-50 years).

Loneliness, low education, and adverse parenting, as well as chronic somatic illnesses, such as cardiovascular disease, diabetes, asthma, and obesity may increase the risk for a lifetime diagnosis of anxiety.

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Table 6 Common risk factors in patients with anxiety and related disorders

- Family history of anxiety [33]
- Personal history of anxiety or mood disorder [34,35]
- Childhood stressful life events or trauma [36,37]
- Being female [4,9]
- Chronic medical illness [34,40]
- Behavioral inhibition [41,42]

CONDUCT DIFFERENTIAL DIAGNOSIS

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COMORBID MEDICAL AND PSYCHIATRIC DISORDERS

Anxiety and related disorders frequently co-occur with other psychiatric disorders.

More than half of patients with an anxiety disorder have multiple anxiety disorders, and almost 30% will have three or more comorbid anxiety or related disorders.

Anxiety is often comorbid with substance use and mood disorders.

An estimated 52% of patients with bipolar disorder, 60% of patients with MDD, and 47% of those with ADHD will have a comorbid anxiety or related disorder.

Therefore, anxiety disorders should be considered in these patients.

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COMORBID MEDICAL AND PSYCHIATRIC DISORDERS

The high frequency of comorbidity must be considered when diagnosing anxiety and related disorders since this can have important implications for diagnosis and treatment.

Anxiety disorders comorbid with other anxiety or depressive disorders are associated with poorer treatment outcomes, greater severity and chronicity, more impaired functioning, increased health service use, and higher treatment costs.

The impact tends to increase with an increasing number of comorbid conditions.

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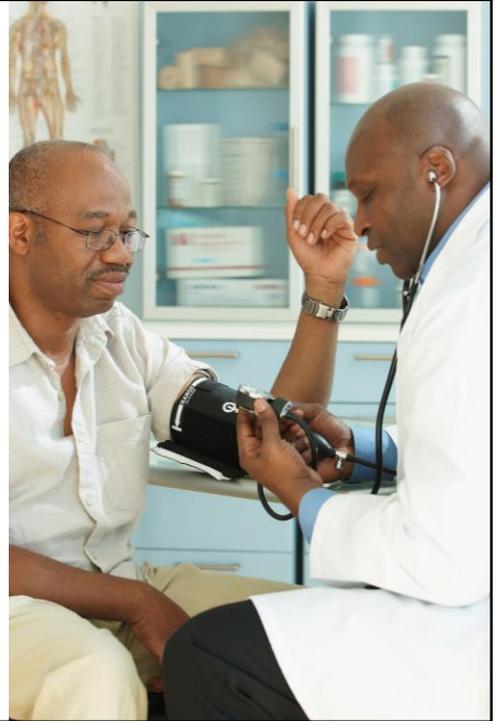
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COMORBID MEDICAL AND PSYCHIATRIC DISORDERS

Patients with anxiety disorders have a higher prevalence of hypertension and other cardiovascular conditions, gastrointestinal disease, arthritis, thyroid disease, respiratory disease, migraine headaches, and allergic conditions compared to those without anxiety disorders.

Comorbid anxiety and related disorders have a significant impact on quality of life (QoL) in patients with medical conditions.

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BASELINE ASSESSMENT

Baseline assessment should include a review of systems, prescribed medications, over-the-counter agents, alcohol use, caffeine intake, and illicit drug use, in addition to evaluation of the anxiety symptoms and functioning.

Table 7 lists potential investigations that can be considered based on an individual patient's presentation and specific symptoms (e.g., dizziness or tachycardia).

Ideally, a physical examination and baseline laboratory investigations should be performed before pharmacotherapy is initiated, with repeat assessments according to best practice guidelines.

Patients with anxiety and related disorders should be monitored initially every one to two weeks and then every four weeks for weight changes and adverse effects of medications, as this is a major factor contributing to discontinuation of medication.

Closer monitoring may be required in children younger than 10 years of age, older or medically ill patients, patients on medications associated with metabolic changes, and those on multiple medications.

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BASELINE ASSESSMENT

Table 7 Considerations for baseline laboratory investigations (as needed based on patient's presenting symptoms)

Basic lab tests

- Complete blood count
- Fasting lipid profile (TC, vLDL, LDL, HDL, TG)
- Electrolytes
- Fasting glucose
- Thyroid-stimulating hormone
- Liver enzymes

If warranted

- Urine toxicology for substance use

Adapted from references [32,53]. HDL = high density lipoprotein; LDL = low density lipoprotein; TC = total cholesterol; TG = triglyceride; vLDL = very low density lipoprotein.

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PSYCHOLOGICAL AND PHARMACOLOGICAL TREATMENT

All patients should receive education about their disorder, efficacy (including expected time to onset of therapeutic effects) and tolerability of treatment choices, aggravating factors, and signs of relapse.

Information on self-help materials such as books or websites may also be helpful.

The choice of psychological or pharmacological treatment depends on factors such as patient preference and motivation, ability of the patient to engage in the treatment, severity of illness, clinicians' skills and experience, availability of psychological treatments, patient's prior response to treatment, and the presence of comorbid medical or psychiatric disorders.

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OVERVIEW OF PSYCHOLOGICAL TREATMENT

Psychological treatments play an important role in the management of anxiety and related disorders.

Regardless of whether formal psychological treatment is undertaken, patients should receive education and be encouraged to face their fears.

Meta-analyses have demonstrated the efficacy of psychological treatments in group and individual formats in patients with panic disorder, specific phobia, SAD, OCD, GAD, or PTSD, particularly exposure-based and other cognitive behavioral therapy (CBT) protocols, as well as mindfulness-based cognitive therapy (MBCT).

When choosing psychological treatments for individual patients, the forms of therapy that have been most thoroughly evaluated in the particular anxiety or related disorder should be used first.

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OVERVIEW OF PSYCHOLOGICAL TREATMENT

CBT is not a single approach to treatment, but rather a process that focuses on addressing the factors that caused and maintain the individual patient's anxiety symptoms.

Some of the core components of CBT are shown in Table 9.

CBT can be effectively delivered as individual or group therapy for most anxiety and related disorders.

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In addition, a variety of self-directed or minimal intervention formats (e.g., bibliotherapy/self-help books, or internet/ computer-based programs with or without minimal therapist contact) have demonstrated significant improvements in anxiety symptoms.

Meta-analyses have also shown that exposure therapy can be effectively administered in a virtual reality format.

These strategies may be particularly useful in cases where real-life exposure is difficult due to inconvenience, expense, or patient reluctance.

OVERVIEW OF PSYCHOLOGICAL TREATMENT

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Table 9 Components of cognitive behavioral interventions

Exposure	<ul style="list-style-type: none"> • Encourage patients to face fears • Patients learn corrective information through experience • Extinction of fear occurs through repeated exposure • Successful coping enhances self-efficacy
Safety response inhibition	<ul style="list-style-type: none"> • Patients restrict their usual anxiety-reducing behaviors (e.g., escape, need for reassurance) • Decreases negative reinforcement • Coping with anxiety without using anxiety-reducing behavior enhances self-efficacy
Cognitive strategies	<ul style="list-style-type: none"> • Cognitive restructuring, behavioral experiments, and related strategies target patients' exaggerated perception of danger (e.g., fear of negative evaluation in SAD) • Provides corrective information regarding the level of threat • Can also target self-efficacy beliefs
Arousal management	<ul style="list-style-type: none"> • Relaxation and breathing control skills can help patient control increased anxiety levels
Surrender of safety signals	<ul style="list-style-type: none"> • Patient relinquishes safety signals (e.g., presence of a companion, knowledge of the location of the nearest toilet) • Patients learn adaptive self-efficacy beliefs

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OVERVIEW OF PSYCHOLOGICAL TREATMENT

Psychotherapy and pharmacotherapy generally demonstrate about equivalent efficacy for the treatment of most anxiety and related disorders.

Results with combination therapy vary for the different anxiety disorders, and results have been conflicting.

Therefore, current evidence does not support the routine combination of CBT and pharmacotherapy as initial treatment.

However, when patients do not benefit from CBT or have a limited response, a trial of pharmacotherapy is advisable.

Similarly, patients who show limited benefit from pharmacotherapy may benefit from CBT.

All patients being treated with pharmacotherapy should be instructed to gradually face their fears (exposure to decrease avoidance).

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SECTION B: PSYCHOPHARMACOLOGY FOR ANXIETY DISORDERS

Discuss the pharmacological interventions for anxiety disorders including:

- **Tricyclics, tetracyclics, and monoamine oxidase inhibitors**
- **Antidepressants**
- **Benzodiazepines**
- **Anticonvulsants**
- **Atypical antipsychotics**
- **Other treatments**

Develop a monitoring system to evaluate the effectiveness and tolerance of pharmacotherapy and strategies for minimizing adverse reactions.

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OVERVIEW OF PHARMACOLOGICAL TREATMENT

Table 10 shows medications that have Health Canada approved indications for use in different anxiety and related disorders.

Various antidepressants including selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), noradrenergic and specific serotonergic antidepressants (NaSSAs), tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), and reversible inhibitors of monoamine oxidase A (RIMAs) have demonstrated some efficacy in the treatment of anxiety and related disorders.

SSRIs and SNRIs are usually preferred as initial treatments, since they are generally safer and better tolerated than TCAs or MAOIs.

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Table 1 Levels of evidence

- 1 Meta-analysis or at least 2 randomized controlled trials (RCTs) that included a placebo condition
- 2 At least 1 RCT with placebo or active comparison condition
- 3 Uncontrolled trial with at least 10 subjects
- 4 Anecdotal reports or expert opinion

Levels of evidence do not assume positive or negative or equivocal results, they merely represent the quality and nature of the studies that have been conducted.

Level 1 and Level 2 evidence refer to treatment studies in which randomized comparisons are available. Recommendations involving epidemiological or risk factors primarily arise from observational studies, hence the highest level of evidence for these is usually Level 3. Recommendations, such as principles of care, reflect consensus opinion based on evidence from various data sources, and therefore are primarily Level 4 evidence.

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Table 2 Treatment recommendation summary

First-line	Level 1 or Level 2 evidence plus clinical support for efficacy and safety
Second-line	Level 3 evidence or higher plus clinical support for efficacy and safety
Third-line	Level 4 evidence or higher plus clinical support for efficacy and safety
Not recommended	Level 1 or Level 2 evidence for lack of efficacy

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Table 10 Medications with Health Canada–approved indications for anxiety and related disorders

	Anxiety disorders	Panic disorder	Social anxiety disorder	Obsessive–compulsive disorder	Generalized anxiety disorder	Posttraumatic stress disorder
ANTIDEPRESSANTS						
SSRIs						
Escitalopram (Ciprallex [®])				X	X	
Fluoxetine (Prozac [®])				X		
Fluvoxamine (Luvox [®])				X		
Paroxetine (Paxil [®])		X	X	X	X	X
Paroxetine CR (Paxil [®] CR)		X	X			
Sertraline (Zoloft [®])		X		X		
TCA						
Clomipramine				X		
Other antidepressants						
Venlafaxine XR (Effexor [®] XR)		X	X		X	
Duloxetine (Cymbalta [®])					X	
AZAPIRONES						
Buspirone (BuSpar [®] , Bupirex [®])					X	
BENZODIAZEPINES*	X					

Data from respective Canadian product monographs [84].

*Multiple generic and brand name products, consult product monographs: alprazolam, bromazepam, chlordiazepoxide, clorazepate, diazepam, lorazepam, and oxazepam are indicated for anxiety disorders; alprazolam is also indicated for panic disorder.

CR = controlled release; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant; XR = extended release.

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OVERVIEW OF PHARMACOLOGICAL TREATMENT

Benzodiazepines may be useful as adjunctive therapy early in treatment, particularly for acute anxiety or agitation, to help patients in times of acute crises, or while waiting for onset of adequate efficacy of SSRIs or other antidepressants.

Due to concerns about possible dependency, sedation, cognitive impairment, and other side effects, benzodiazepines should usually be restricted to short-term use, and generally dosed regularly rather than as-needed.

Several anticonvulsants and atypical antipsychotics have demonstrated efficacy in some anxiety and related disorders, but for various reasons, including side effects, as well as limited randomized controlled trial (RCT) data and clinical experience, these agents are generally recommended as second-line, third-line, or adjunctive therapies.

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OVERVIEW OF PHARMACOLOGICAL TREATMENT

The choice of medication should take into consideration the evidence for its efficacy and safety/tolerability for the treatment of the specific anxiety and related disorder, as well as for any comorbid conditions the patient might have, in both acute and long-term use.



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ANTIDEPRESSANTS

Antidepressants are the cornerstone of pharmacological treatment for anxiety disorders.

The guidelines recommend SSRIs and SNRIs as first-line agents across most anxiety disorders because of their strong evidence for efficacy, tolerability, and safety.

These include medications such as escitalopram, (paroxetine), sertraline, venlafaxine XR, and duloxetine.

Tricyclic antidepressants (TCAs) such as clomipramine and imipramine are effective but considered second-line due to their side-effect burden and lower tolerability.

Clomipramine remains an important option in obsessive-compulsive disorder.

Tetracyclics (e.g., mirtazapine) and monoamine oxidase inhibitors (MAOIs) are also effective for some patients but are generally reserved for second- or third-line use because of dietary restrictions, drug interactions, and tolerability issues.

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BENZODIAZEPINES

Benzodiazepines have well-established anxiolytic efficacy and are recommended as second-line treatments for most anxiety disorders.

They may be considered in patients who cannot tolerate or have not responded to first-line agents.

However, they are not recommended as first-line due to the risks of sedation, dependence, withdrawal, and cognitive impairment.

In posttraumatic stress disorder, benzodiazepines are explicitly not recommended because of lack of efficacy and potential harm.

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ANTICONVULSANTS

Certain anticonvulsants have demonstrated efficacy in anxiety disorders, though evidence is more limited compared to antidepressants.

According to the 2014 Canadian Clinical Practice Guidelines, pregabalin is recommended as a first-line treatment for generalized anxiety disorder (GAD) and Social Anxiety Disorder (SAD) due to its demonstrated efficacy and tolerability.



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ATYPICAL ANTIPSYCHOTICS

Atypical antipsychotics are not recommended as first-line treatments for any anxiety disorder.

Instead, they are considered adjunctive or third-line options for treatment-resistant cases when standard treatments have failed.

Agents such as quetiapine XR have the strongest evidence, particularly in generalized anxiety disorder, but they should be used cautiously due to potential risks.

Their use is limited by adverse effects such as sedation, weight gain, and metabolic syndrome, so careful monitoring is required.

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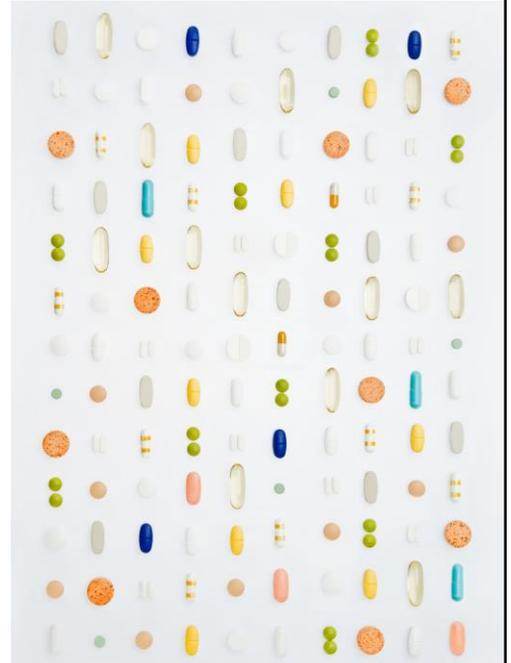
OTHER AGENTS

The guidelines also discuss a range of other pharmacological agents with varying levels of evidence.

Bupirone may be useful in generalized anxiety disorder and is generally considered a second-line treatment.

Hydroxyzine has demonstrated some efficacy in reducing acute anxiety symptoms, but it is not recommended for long-term management.

Beta-blockers such as propranolol can help reduce peripheral autonomic symptoms, particularly in performance anxiety, but they do not address the core features of most anxiety disorders.



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CANADIAN TREATMENT GUIDELINES REVIEW

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PHARMACOLOGICAL TREATMENTS — GENERALIZED ANXIETY DISORDER (GAD)

Pharmacotherapeutic approaches should begin with one of the first-line options including an SSRI such as escitalopram, paroxetine, or sertraline, an SNRI such as duloxetine or venlafaxine XR, or other antidepressant such as agomelatine.

The anticonvulsant pregabalin is also a recommended first-line therapy. If response to optimal doses is inadequate or the agent is not tolerated, therapy should be switched to another firstline agent before considering second-line medications.

Second-line choices include bupropion XL, buspirone, hydroxyzine, imipramine, quetiapine XR, vortioxetine, as well as the benzodiazepines, alprazolam, brom

Third-line agents, adjunctive therapies, as well as biological and alternative therapies may be useful when patients fail to respond to an optimal treatment trial of first- and second-line therapies used alone and in combination with azepam, diazepam, and lorazepam.

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Table 23 Strength of evidence for pharmacotherapy for GAD

Agent	Level of evidence	Agent	Level of evidence
Antidepressants			
SSRIs		TCA	
Escitalopram [544-552]	1	Imipramine [553,581-583]	1
Paroxetine [546,547,553-558]	1	Other antidepressants	
Sertraline [556,559-561]	1	Agomelatine [584,585]	1
Citalopram [562]	3	Vortioxetine [586,587]	1*
Fluoxetine [563]	3	Bupropion XL [549]	2
Paroxetine CR [564,565]	3	Trazodone [583]	2
SNRIs		Mirtazapine [588]	3
Duloxetine [566-571]	1		
Venlafaxine XR [548,553,570-580]	1		
Other therapies			
Anxiolytics		Atypical antipsychotics	
Benzodiazepines		Quetiapine XR [551,557,602,603]	1
Alprazolam [589-593]	1	Adjunctive quetiapine [565,604,605]	1*
Bromazepam [589,594]	1	Adjunctive risperidone [606,607]	1*
Diazepam [583,589,595,596]	1	Adjunctive olanzapine [608]	2
Lorazepam [589,593,597-601]	1	Adjunctive aripiprazole [269,609]	3
		Adjunctive quetiapine XR [610]	3
		Adjunctive or monox ziprasidone [611,612]	2 (-ve)
Anticonvulsants		Other treatments	
Pregabalin [576,577,592,593,597,613]	1	Buspirone [108,561,572,589,598,618,619]	1
Divalproex chrono [614]	2	Hydroxyzine [594,619,620]	1
Tiagabine [615,616]	1 (-ve)	Pexacerfont [552]	2 (-ve)
Adjunctive pregabalin [617]	2	Propranolol [621]	2 (-ve)
		Memantine [622]	4 (-ve)

*Conflicting data. SNRI = serotonin-norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant; XL = extended release; XR=extended release; (-ve) = negative.

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Table 24 Recommendations for pharmacotherapy for GAD

First-line	Agomelatine, duloxetine, escitalopram, paroxetine, paroxetine CR, pregabalin, sertraline, venlafaxine XR
Second-line	Alprazolam*, bromazepam*, bupropion XL*, buspirone, diazepam*, hydroxyzine, imipramine, lorazepam*, quetiapine XR*, vortioxetine
Third-line	Citalopram, divalproex chrono, fluoxetine, mirtazapine, trazodone
Adjunctive therapy	Second-line: pregabalin Third-line: aripiprazole, olanzapine, quetiapine, quetiapine XR, risperidone Not recommended: ziprasidone
Not recommended	Beta blockers (propranolol), pexacerfont, tiagabine

CR = controlled release; XL = extended release; XR=extended release.

*Note: These have distinct mechanisms, efficacy and safety profiles. Within these second-line agents, benzodiazepines would be considered first in most cases, except where there is a risk of substance abuse, while bupropion XL would likely be reserved for later. Quetiapine XR remains a good choice in terms of efficacy, but given the metabolic concerns associated with atypical antipsychotic, it should be reserved for patients who cannot be provided antidepressants or benzodiazepines. Please refer to text for further rationale for the recommendations.

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PHARMACOLOGICAL TREATMENTS — PANIC DISORDER (PD) AND AGORAPHOBIA

First-line options for the treatment of panic disorder include citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, venlafaxine XR, escitalopram, or paroxetine CR.

Second-line choices include the TCAs (clomipramine and imipramine), mirtazapine, reboxetine, or benzodiazepines (alprazolam, clonazepam, lorazepam, and diazepam).

Third-line agents, adjunctive therapies, as well as biological and alternative therapies may be useful when patients fail to respond to an optimal treatment trial of first- and second-line therapies used alone and in combination.

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Table 14 Strength of evidence for pharmacotherapy for panic disorder

Agent	Level of evidence	Agent	Level of evidence
Antidepressants			
SSRIs			
Citalopram [198-200]	1	TCAs	
Fluoxetine [201-204]	1	Clomipramine [199,211,213,232,233]	1
Fluvoxamine [195,205-210]	1	Imipramine [207,224,233-240]	1
Paroxetine [211-219]	1	MAOIs and RIMAs	
Sertraline [183,220-224]	1	Phenelzine [240]	2
Escitalopram [198]	2	Moclobemide [204,232,241,242]	1*
Paroxetine CR [225]	2	Tranylcypromine [243]	3
Other antidepressants			
SNRIs			
Venlafaxine XR [215,216,227-229]	1	Reboxetine [200,219,244]	1
Duloxetine [230]	3	Mirtazapine [203,245,246]	2
Milnacipran [231]	3	Bupropion SR [247,248]	3*
Other therapies			
Anxiolytics			
Benzodiazepines			
Alprazolam [234,249-254]	1	Atypical antipsychotics	
Clonazepam [218,250,255-258]	1	Risperidone [217,267]	2
Lorazepam [251,259,260]	1	Olanzapine [268]	3
Diazepam [261-263]	1	Quetiapine [267]	3
Adjunctive clonazepam [264,265]	1	Adjunctive aripiprazole [269]	3
Adjunctive alprazolam ODT [266]	3	Adjunctive olanzapine [270]	3
Other treatments			
Bupropion [254,282]	1 (-ve)	Adjunctive risperidone [271]	3
Trazodone [283]	2 (-ve)	Anticonvulsants	
Propranolol [262,284,285]	2 (-ve)	Divalproex [272-275]	3
Adjunctive pindolol [286]	2	Levetiracetam [276]	3
		Gabapentin [277]	2 (-ve) [†]
		Tiagabine [278,279]	2 (-ve)
		Carbamazepine [280]	3 (-ve)
		Adjunctive divalproex [281]	3

*Conflicting data. †No significant superiority over placebo in overall population, but significant benefits in subgroup of more severely ill patients. CR = controlled release; MAOI = monoamine oxidase inhibitor; ODT = orally disintegrating tablets; RIMA = reversible inhibitor of monoamine oxidase A; SNRI = serotonin-norepinephrine reuptake inhibitor; SR = sustained release; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant; XR = extended release; (-ve) = negative.

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Table 15 Recommendations for pharmacotherapy for panic disorder

First-line	Citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, paroxetine CR, sertraline, venlafaxine XR
Second-line	Alprazolam, clomipramine, clonazepam, diazepam, imipramine, lorazepam, mirtazapine, reboxetine
Third-line	Bupropion SR, divalproex, duloxetine, gabapentin, levetiracetam, milnacipran, moclobemide, olanzapine, phenelzine, quetiapine, risperidone, tranylcypromine
Adjunctive therapy	Second-line: alprazolam ODT, clonazepam Third-line: aripiprazole, divalproex, olanzapine, pindolol, risperidone
Not recommended	Bupropion, propranolol, tiagabine, trazodone

CR = controlled release; ODT = orally disintegrating tablets; SR = sustained release; XR = extended release.

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PHARMACOLOGICAL TREATMENTS — SOCIAL ANXIETY DISORDER (SAD)

Pharmacotherapeutic approaches should begin with a first-line antidepressant such as escitalopram, fluvoxamine, fluvoxamine CR, paroxetine, paroxetine CR, sertraline, or venlafaxine XR, or the anticonvulsant pregabalin.

Second-line choices include the benzodiazepines alprazolam, bromazepam, and clonazepam, as well as citalopram, gabapentin, and phenelzine. Pregabalin has also been shown to maintain benefits and prevent relapse in a six-month study.

Third-line agents and adjunctive therapies may be useful when patients fail to respond to optimal treatment trials of first- and second-line therapies used alone and in combination.

Integration with CBT is strongly recommended to optimize outcomes.

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Table 20 Strength of evidence of pharmacotherapy for SAD

Agent	Level of evidence	Agent	Level of evidence
Antidepressants			
SSRIs [58,626-629]			
Escitalopram [430-432]	1	TCAs	
Fluvoxamine [433-435]	1	Clomipramine [458,459]	3
Fluvoxamine CR [436-437]	1	Imipramine [460]	3 (-ve)
Paroxetine [431,438-444]	1	MAOIs and RIMAs	
Sertraline [445-448]	1	Phenelzine [384,386,418,461,462]	1
Fluoxetine [382,387,449]	1*	Noclobemide [417,462-466]	1*
Citalopram [450,451]	2	Other antidepressants	
Paroxetine CR [452]	2	Mirtazapine [467,468]	1*
Adjunctive paroxetine [453]	3	Bupropion SR [469]	3
SNRIs			
Venlafaxine XR [439,441,454,255,456]	1		
Duloxetine [457]	2		
Other therapies			
Anxiolytics			
Benzodiazepines			
Clonazepam [385,470,471]	1	Anticonvulsants	
Alprazolam [386]	2	Pregabalin [474,475]	1
Bromazepam [472]	2	Gabapentin [476,477]	2
Adjunctive clonazepam [473]	2 (-ve)	Levetiracetam [478-480]	2 (+ve)
		Divalproex [481]	3
		Tiagabine [477,482]	3
		Topiramate [483]	3
Other treatments			
Atenolol [461,484]	1 (-ve)	Atypical antipsychotics	
Buspirone [383,485]	1 (-ve)	Clanzapine [493]	2
Atomoxetine [486,487]	1*	Quetiapine [494,495]	2 (-ve)
Propranolol [488]	2 (-ve)	Adjunctive aripiprazole [496]	3
Selegiline [489]	3	Adjunctive risperidone [271]	3
Pergolide [490]	3 (-ve)		
Adjunctive buspirone [491]	3		
Adjunctive pindolol [492]	2 (-ve)		

*Conflicting data. CR = controlled release; MAOI = monoamine oxidase inhibitor; RIMA = reversible inhibitor of monoamine oxidase A; SNRI = serotonin-norepinephrine reuptake inhibitor; SR = sustained release; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant; XR = extended release; (-ve) = negative.

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Table 21 Recommendations for pharmacotherapy for SAD

First-line	Escitalopram, fluvoxamine, fluvoxamine CR, paroxetine, paroxetine CR, pregabalin, sertraline, venlafaxine XR
Second-line	Alprazolam, bromazepam, citalopram, clonazepam, gabapentin, phenelzine
Third-line	Atomoxetine, bupropion SR, clomipramine, divalproex, duloxetine, fluoxetine, mirtazapine, moclobemide, olanzapine, selegiline, tiagabine, topiramate
Adjunctive therapy	Third-line: aripiprazole, buspirone, paroxetine, risperidone Not recommended: clonazepam, pindolol
Not recommended	Atenolol ^a , buspirone, imipramine, levetiracetam, propranolol ^a , quetiapine

CR = controlled release; SR = sustained release; XR = extended release.

^aBeta-blockers have been successfully used in clinical practice for performance situations such as public speaking.

Note: although there is limited evidence for citalopram in SAD, it is likely as effective as the other SSRIs, in contrast there are negative trials of fluoxetine in SAD suggesting it may be less effective than other SSRIs [382,449].

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SPECIFIC PHOBIAS — PHARMACOLOGY



Pharmacotherapy is rarely the first-line treatment for specific phobias.



SSRIs may be considered in severe or disabling cases, particularly when comorbid anxiety exists.



However, exposure-based cognitive-behavioral therapy remains the treatment of choice, with the most robust evidence for long-term symptom reduction.

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CHILDREN AND ADOLESCENTS

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Table 33 Strength of evidence of treatments for anxiety and related disorders in children and adolescents

Disorder	Antidepressants	Benzodiazepines and other treatments
OCD	Fluoxetine (Level 1) [1264-1269] Clomipramine (Level 1) [1274-1276] Citalopram (Level 2) [1264,1270] Fluvoxamine (Level 2) [1271] Paroxetine (Level 2) [1272] Sertraline (Level 2) [1273]	Antipsychotics Adjunctive aripiprazole (Level 3) [1293] Other Riluzole (Level 4) [1294]
Panic disorder		Anxiolytics Clonazepam (Level 4) [1287,1288] Alprazolam (Level 4) [1289]
SAD	Fluoxetine (Level 1) [1227,1277] Fluvoxamine (Level 2) [1278] Paroxetine (Level 2) [1279] Venlafaxine XR (Level 2) [1282] Escitalopram (Level 3) [1280] Sertraline (Level 3) [1281] Mirtazapine (Level 3) [1283]	Anxiolytics Alprazolam (Level 2, -ve) [1290]
Separation anxiety disorder	Fluoxetine (Level 2) [1277] Fluvoxamine (Level 2) [1278]	Anxiolytics Clonazepam (Level 2, -ve) [1292]
GAD	Fluoxetine (Level 2) [1277] Fluvoxamine (Level 2) [1278] Sertraline (Level 2) [1284]	Anxiolytics Alprazolam (Level 2, -ve) [1290]
School-refusal	Citalopram (Level 4) [1285] Adjunctive imipramine (Level 2) [1259]	Anxiolytics Alprazolam (Level 2, -ve) [1291]
PTSD	Sertraline (Level 2, -ve) [1286] Adjunctive sertraline (Level 2, -ve) [946]	

XR = extended release; (-ve) = negative.

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SAFETY AND SIDE EFFECTS

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MONITORING ADVERSE REACTIONS

Each medication class has specific adverse effects that require monitoring:

- **SSRIs and SNRIs:** gastrointestinal symptoms, sexual dysfunction, insomnia.
 - **Benzodiazepines:** sedation, psychomotor slowing, dependence.
 - **Atypical antipsychotics:** metabolic syndrome, weight gain, extrapyramidal effects.
 - **Anticonvulsants:** hepatic and hematological side effects (drug-specific).
- Start medications at low doses, titrate slowly, and adjust based on age, comorbidities, or concurrent substance use.

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**SELECTIVE
SEROTONIN
REUPTAKE
INHIBITORS (SSRI)
ADVERSE EFFECTS**

THE NEW AGE

Tremor

Headache

Euphoria

Nervousness

(dizziness, insomnia, agitation, akathisia, discontinuation symptoms, serotonin syndrome)

Endocrine (SiADH, galactorrhea), osteoporosis

Weight changes

Anorgasmia

GI upset, GI bleeding

Excretions (diaphoresis, rhinitis)

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**SEROTONIN-
NOREPINEPHRINE
REUPTAKE
INHIBITOR (SNRI)
ADVERSE EFFECTS**

DAD SINGS

Diastolic increase in BP

Anorexia

Dry mouth

Sexual dysfunction

Insomnia

Nervousness

GI side effects

Sweating

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TRICYCLIC ANTIDEPRESSANTS (TCA) ADVERSE EFFECTS

NO BOWEL SOUNDS
Nausea and vomiting
Obesity
Blurred vision
Orthostatic hypotension
Widening QRS, increased QTc (also reported increased PR, decreased ST and blunted T wave)
Ejaculatory disturbances
Lethargy
Sinus tachycardia
Overdose
Urinary hesitance
Narrow angle glaucoma precipitation
Dry mucous membranes
Seizure threshold decrease

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ANXIOLYTICS

The most common side effects associated with benzodiazepines include primarily sedation, fatigue, ataxia, slurred speech, memory impairment, and weakness.

Benzodiazepines are associated with withdrawal reactions, rebound, and dependence, with the risk being greater with short- and intermediate-acting compared to long-acting agents.

These agents should be used with caution in patients with SUDs.

Older patients (generally over 65 years of age) may be at high risk for falls and fractures due to psychomotor impairment associated with benzodiazepines. Cognitive impairment has been reported, some of which may persist after cessation of therapy.

In particular, memory impairment has been associated with high-dose or high-potency benzodiazepines, particularly in older people.

Reported side effects of azapirones (buspirone) include dizziness, drowsiness, and nausea.

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ANTIPSYCHOTIC ADVERSE EFFECTS

(MORE D2)

RESHAPE

Rhinitis

EPS

Sedation

Headache, hyperlipidemia

Appetite/weight changes, agitation

PRL increase

Edema

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ANTIPSYCHOTIC ADVERSE EFFECTS

(LESS D2)

SAD COST

Sedation

Appetite/weight changes

Diabetes, DKA, dry mouth

Constipation

Orthostatic hypotension

Seizure

Triglyceride increase, ALT
increase

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ANTICONVULSANTS

Anticonvulsants are associated with gastrointestinal side effects, somnolence, weight gain, tremor, as well as dermatologic and hematologic side effects.

In addition, several anticonvulsants have a potential risk of serious rash, erythema multiforme, Stevens-Johnson syndrome, or toxic epidermal necrolysis.

Regular monitoring of serum medication levels and liver function is required for patients on divalproex.

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FOLLOW-UP

Anxiety and related disorders are often chronic and a systematic approach to treatment should include patient education, assessment of comorbidities, and evidence based pharmacological and psychological interventions with adequate monitoring and duration.

Pharmacological treatment is often associated with a delay of about two to eight weeks in onset of symptom relief, with full response taking up to 12 weeks or more.

Longer-term therapy has been associated with continued symptomatic improvement and the prevention of relapse, and therapy should be continued for at least 12-24 months for most patients.

It is imperative to be mindful of drug-drug interactions and metabolism considerations, as significant level changes or adverse effects can be challenging to manage in a patient with already heightened vigilance to physical sensations

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FOLLOW-UP

Medication should be initiated at low doses and titrated to the recommended dosage range at one- to two-week intervals over four to six weeks.

Once the therapeutic range has been achieved, improvement is usually seen over the next four to eight weeks.

Follow up should occur at two-week intervals for the first six weeks and monthly thereafter.

For a patient undergoing psychotherapy, the treatment schedule is structured around weekly contact with a therapist for about 12-20 weeks, although shorter protocols and minimal intervention programs have also proven effective.

A follow up appointment four weeks later and then every two to three months is usually sufficient.

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ASSESSING RESPONSE TO TREATMENT

Therapy should seek to improve symptoms and distress.

The optimal goal is full remission of symptoms and return to a premorbid level of functioning.

However, goals may need to be individualized for some patients with disorders that have been present since childhood as they may never have had adequate premorbid functioning.

A response to therapy is often defined as a percentage reduction in symptoms (usually 25-50%) on an appropriate scale.

Remission is often defined as loss of diagnostic status, a pre-specified low score on an appropriate disorder-specific scale, and no functional impairment in fully recovered patients as measured by a scale such as the Sheehan Disability Scale or SF-36.

Effectiveness should be evaluated regularly using standardized scales as shown earlier

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