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Introduction

Anxiety disorders are the most prevalent types of psychiatric disorders in the USA, affecting both children and adults at staggering rates. Recognition of these disorders in the primary care setting can set the stage for timely diagnosis and appropriate therapeutic interventions as well as prevent potential misdiagnosis of mental illnesses with overlapping symptoms. There can be significant distress and impairment associated with anxiety disorders, and effective treatment can be life changing. Given the targeted nature of this text, this chapter will focus on the anxiety disorders that are most likely to be encountered in the pediatric primary care setting: social anxiety disorder, separation anxiety disorder, and generalized anxiety disorder.

Brief Review of Epidemiology and Pathophysiology

In the USA, anxiety disorders are the most common psychiatric conditions in both adults and children, affecting roughly 40 million Americans [1–3]. Though anxiety disorders are very treatable, only one-third of those suffering from an anxiety disorder receive treatment [4]. Moreover, 25% of adolescents will be diagnosed with an anxiety disorder in his or her lifetime [5]. Though anxiety symptomology is relatively consistent in its phenotypic expression, there are undoubtedly variations in the manifestation of these symptoms in children and adolescents for a number of reasons including developmental factors, cognitive factors, differences in child-specific antecedents (“triggers”)/maintenance factors, and other factors that vary from patient to patient.

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Diagnosis and Key Components of History

Anxiety disorders share more commonalities in presentation than disparities. Thus, children and adolescents presenting with separation anxiety, social anxiety, and worry (GAD) often present in a consistent fashion. All three of these disorders are often manifested through school refusal or premature departure from school [6], somatic complaints (stomachaches, heart palpitations, hot/cold flushes), irritability, sleep disturbance, restlessness, frequent reassurance seeking toward their parents, and avoidance behavior [6].

Significant alteration from previous observations of functioning is an important component to identify when assessing the child or adolescent's history since caregiver report is essential in aiding diagnosis. Since children of anxious parents are three to seven times more likely than children of non-anxious parents to have an anxiety disorder [1, 7, 8], being mindful of parental anxiety and potential parental modeling of distress is an important consideration when assessing child anxiety. Diagnostic criteria for all anxiety and related disorders require the symptoms to cause significant distress and impairment.

Separation Anxiety Disorder

Separation anxiety disorder is characterized by excessive anxiety about being away from a loved one, particularly a caregiver. The child is often worried about a negative event happening to the caregiver or a negative event happening to the child. A child with normal separation concerns may express "missing" the caregiver when he/she goes on an extended business trip, whereas a child suffering from separation anxiety frets about the absence of a caregiver for an extended period of time on a frequent basis, even during the most mundane situations (e.g., if the child is invited to a sleepover, the child is at school and parent is driving several hours away for work, or the parent is away from the child for a few hours). The child with separation anxiety may also frequently worry about being kidnapped or refuse to attend school due to anxiety about something bad happening to the caregiver. Additionally, the child with separation anxiety may also experience nightmares and seek frequent reassurance about the parent's whereabouts.

Social Anxiety Disorder

Social anxiety disorder involves a persistent fear and anxiety about social situations where negative evaluation may occur. Though it is normal to be wary of strangers and novel situations (such as when meeting a new person or being nervous about speaking in front of the class), the socially anxious child may do any of the following: cry excessively about presenting in front of the class to the point of being sick and not attending school, avoid sporting events due to anxiety about being made fun of by peers, have very little social interaction with peers in general, and complain of

somatic complaints weeks in advance before a presentation. Social anxiety may also manifest as significant performance anxiety before participating in sporting though the socially anxious child “plays well” during practice.

Generalized Anxiety Disorder

Generalized anxiety disorder is characterized by significant anxiety that leads to excessive worry. Normal concerns that are not driven by chronic levels of anxiety lead to effective problem solving. For example, a child experiencing normal levels of anxiety may worry about an upcoming exam but view the anxiety as an emotion that is helpful by prompting the child to study. However, the child with chronic worry may worry about a number of areas, even if things are going well. For example, the worried child may worry about getting to school on time, worry about making mistakes on assignments, become “frozen” when making everyday decisions, and seek frequent reassurance from a caregiver about whether he/she will be able to engage in certain activities when on a trip. The worried child also experiences sleep disturbance, difficulty concentrating, fatigue, and irritability.

Confounders and Comorbidities

Due to the restlessness and impaired concentration often associated with both anxiety and impulsivity, ADHD is a significant differential diagnosis for anxiety in children and adolescents. Though restlessness is a symptom of both ADHD and anxiety, anxiety-associated restlessness is associated with more subjective distress, somatic complaints, and avoidance behaviors. The inattention often found in ADHD tends to be more consistent, particularly in school settings. Difficulty concentrating as a symptom of anxiety, however, tends to be the result of the mind being occupied by worried thoughts about school, loved ones, social relationships, and other factors. Depression is a frequent comorbid diagnosis with anxiety disorders in children and adolescents. Determining whether symptoms of depression are present in addition to anxiety is paramount when assessing the child or adolescent.

Anxiety in children commonly manifests with somatic symptoms such as headaches, abdominal pain, shortness of breath, chest pain, and dizziness. A thorough medical workup should be performed on each patient, and medical problems such as migraine headaches, celiac disease, Gastroesophageal reflux disease (GERD), mitral valve prolapse, asthma, and other medical disorders should be ruled out rather than assuming the symptoms are solely manifestations of anxiety. Comorbidity with such conditions and anxiety can most certainly occur, and children with chronic medical issues are at increased risk for mental illness.

Substance use should always be a consideration. Intoxication with stimulant prescription or street drugs and withdrawal from sedatives such as opiates to benzodiazepines to alcohol can very much mirror anxiety symptoms. If benzodiazepines are being abused, there may even be interdose anxiety that the patient is experiencing.

In certain patients, marijuana use can precede the onset of severe anxiety symptoms [9]. Patients with substance use disorders will many times not have the usual triggers that are associated with typical anxieties in children and adolescents. Symptoms may also be greatly out of proportion to what is typically seen and quite treatment resistant [10].

Screening and Measures

Given the frequent comorbidity of anxiety and depression, screening for the other is recommended whenever there is clinical suspicion of either. Table 11.1 displays commonly used screening assessment tools for anxiety and depression in children and adolescents. Additionally, all youth with anxiety symptoms should be screened for trauma, depression, and substance use disorders. Please refer to Fig. 15.1 in this text's Substance Use Disorder (SUD) chapter for the CRAFFT, the recommended SUD screening tool.

Initial Management

Psychosocial and Behavioral Interventions

Behaviorally, it is important to reiterate the importance of eliminating avoidance behavior when managing anxiety and related disorders in children and adolescents. Avoidance works in the short-term, so it can be very reinforcing. The problem is that it is associated with significant impairment and robs the youth of the opportunity to realize that things would not turn out as badly as the youth thought they would. Thus, attending school, giving speeches in front of classmates, interacting with others, and eliminating worry concerns are necessary targets of treatment. Though the child or adolescent may report that he/she is unable to function in the particular social situation, assure the caregiver that gradual "exposure" back into the currently feared situation will be essential in eliminating significant distress and impairment.

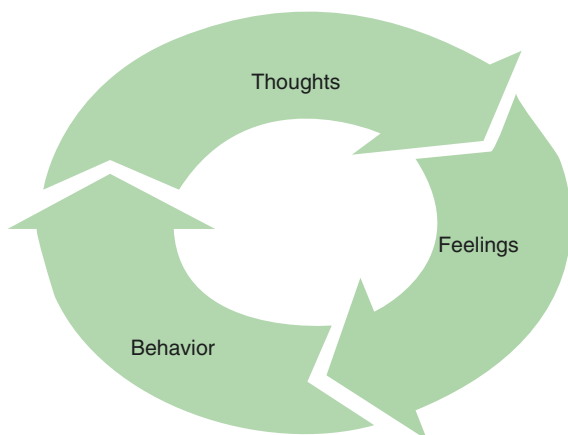
Ideally, this is achieved in collaboration with a mental health professional trained in cognitive behavioral therapy (CBT), the gold standard psychological intervention for anxiety disorders (see Fig. 11.1). Of note, in collaborative care models, depending on licensure, training, and state regulations, the behavioral care manager may be able to initiate psychotherapy. Psychotherapy can be helpful as children who are prone to anxiety and related symptoms struggle in two specific areas: (a) negative, unrealistic thoughts about themselves, their emotions, and the world around them and (b) attempts to avoid anxiety-provoking situations as well as strong, negative emotions. As such, many children with anxiety have thoughts that include "thinking errors" that create more anxiety than necessary in many harmless situations. Examples include "mind reading" (e.g., "they will think I'm an idiot"), fortune telling (e.g., "I'm going to fail the exam"), and catastrophizing (e.g., "this always happens to me!" or "this is the worst paper ever!").

CBT contains an effective treatment component known as cognitive restructuring that teaches the child or adolescent that thoughts are "guesses" not "facts" in

Table 11.1 Public domain anxiety symptom rating scales

Measure	Domain	Age validated and # of items	Completed by	Administration and scoring times training (none, unless otherwise indicated)	Languages available	Reference
Pediatric Symptom Checklist (PSC)	Interpersonal domains, psychosocial dysfunction	4–16 years 35 items	Youth	<5 min scoring 2 min	Translated in >20 languages	[11]
Acute Stress Checklist for Children	Acute stress disorder symptoms w/in the first month of traumatic exposure	8–17 years 29 items	Youth	5 min scoring: 1–2 min	English and Spanish	[12]
Penn State Worry Questionnaire for Children (PSWQ-C)	Worry	7–17 years 14 items	Youth	<5 min scoring: 2 min	English, Korean, Danish	[13]
Revised Children's Anxiety and Depression Scale (RCADS)—Youth and Parent Versions	Anxiety, depression	8–18 years 47 items	Youth and/or parent	5–10 min Excel scoring sheets online available for English versions in children grades 3 and up at http://www.childfirst.ucla.edu/resources.html Hand scoring: 5 min	English, Spanish, Danish, Dutch, Korean	[14]
Screen for Child Anxiety-Related Emotional Disorders (SCARED)—Youth and Parent Versions	Anxiety disorders	8–18 years 41 items	Youth and/or parent	10 min Scoring: 2 to 3 min	Arabic, Chinese, English, French, German, Italian, Portuguese, Spanish, Thai	[15]
Spence Children's Anxiety Scale	Generalized anxiety symptoms (DSM-IV)	8–15 years 45 items Preschool version for ages 2.5–6.5 34 items	Youth and/or parent	5–10 min Adobe reader X automatic scoring questionnaire available at http://www.scaswebsite.com/ Hand scoring: 5 min	English, Spanish, Chinese, Arabic, French, Russian preschool, German, Hindi, Portuguese preschool, and others	[16]

Fig. 11.1 CBT model: the bidirectional relationship between thoughts, feelings/physical sensations, and behaviors



addition to understanding the connections between the thought, feeling/physical sensations, and resultant behaviors. Additionally, Socratic questions can be used to assist the child or adolescent in challenging unhelpful thoughts and creating more flexible thoughts used to ward off anxiety. Examples include “What’s the evidence that this negative event will occur?” “Is the negative prediction being driven by anxiety?” “Is the patient 100% sure this negative outcome will occur?” “What’s the worst that can happen and can the patient cope with that?” “What’s happened in the past?”

Relaxation and mindfulness techniques can be additionally helpful in alleviating much of the physiological arousal associated with anxiety and worry. Of note, this text’s Depression chapter includes a brief discussion of some apps that may be helpful adjuncts in these interventions. A mindfulness approach can be very helpful in assisting a child or adolescent to focus on the present moment rather than engage in worry, avoidance, or other behaviors driven by distressing emotional states. One strategy in assisting the child or adolescent with being more aware of his or her emotion in real time, or anchoring technique, is called nonjudgmental awareness. The child or adolescent begins with a few diaphragmatic breaths (e.g., inhale for 4 s, hold the breath for 5 s, and exhale for 6 s) followed by simply becoming “aware” of one’s thoughts, feelings/physical sensations, and behaviors as they are occurring in the present moment.

Finally, one of the most significant factors in effectively managing anxiety in children and adolescents is to provide the caregivers information about helpful strategies to implement at home. Please see Table 11.2 for key points to include while you are educating the patient’s family.

Table 11.2 Selective serotonin reuptake inhibitors (SSRIs) for anxiety disorders [18–22]

Medication	Initial dose	Target dose	Maximum dose	Clinical considerations
Escitalopram (Lexapro)	5–10 mg	Children 10–20 mg Adolescents 10–20 mg	30 mg	FDA approved for social anxiety disorder from 10 to 17 years old. Generally accepted for effectiveness in GAD, lower risk of drug-drug interactions, intermediate half-life Available in liquid formulation
Fluoxetine (Prozac)	5–10 mg	Children 20 mg Adolescents 20–40 mg	30 mg in younger children 60 mg in adolescents	FDA indication for social anxiety disorder from ages 5 to 18, multiple studies showing effectiveness with GAD. Also approved for treatment of OCD in children 7 and up Long half-life, potential for drug-drug interactions Available in liquid formulation
Fluvoxamine (Luvox)	12.5 mg	Children 50–200 mg Adolescents 50–200 mg	200 mg in patients 8–11 y/o 300 mg in 11 y/o and up	FDA approved for generalized anxiety disorder from 8 to 17 years old. Multiple studies suggest effectiveness in social anxiety disorder and separation anxiety disorder. Drug-drug interactions due to inhibition of CYP1A2, CYP2C9, and CYP3A4. Consider lower doses in female patients. Divide into twice-daily dosing for doses greater than 50 mg per day total dose
Sertraline (Zoloft)	12.5–25 mg	Children 50–200 mg Adolescents 50–200 mg	200 mg	FDA approved for obsessive compulsive disorder from 6 to 17 years old. Multiple studies showing effectiveness in GAD and separation anxiety disorder and social phobia, including the CAM study. Intermediate half-life Available in liquid formulation
Citalopram (Celexa)	2.5–10 mg	Children 20–40 mg Adolescents 20–40 mg	40–60 mg	FDA approved for generalized anxiety disorder from 7 to 17 years old. Considered to be useful in social anxiety disorder and separation anxiety disorder. Fewer drug interactions and fewer side effects, potential for QTc in combination with doses over 40 mg per day or when used with pimozide Available in liquid formulation

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Table 11.2 (continued)

Medication	Initial dose	Target dose	Maximum dose	Clinical considerations
Paroxetine (Paxil)	5–10 mg	Children 10–30 mg Adolescents 20–40 mg	50–60 mg	FDA approved for social anxiety disorder from 8 to 17 years old. Generally considered useful in the treatment of separation anxiety disorder and GAD. Short half-life; higher risk of discontinuation syndrome; requires a slower taper on discontinuation; slightly greater potential for weight gain; <i>may have higher risk of suicidality compared to sertraline and fluoxetine</i> Available in liquid formulation

Pharmacologic Interventions

In the pharmacological treatment of anxiety in children, the goal is to decrease the overall burden of anxiety. While medications are certainly not the center of treatment for children, they can be helpful in decreasing the anxiety to the point where the patient can start to face it in their day-to-day life and deal with it in therapy. In child psychiatry, the mantra for medication treatment is “Start low, go slow.” This helps to minimize potential side effects of medications. Youth with anxiety disorders may be even more distressed by physical side effects than their anxiety disorder, particularly in the window before therapeutic effect has taken place.

Selective serotonin reuptake inhibitor (SSRI) antidepressants are first-line psychiatric medications for anxiety disorders in children and adolescents. Unfortunately, SSRIs and most of the other treatments for anxiety typically do not work immediately, and it is important to set expectations about the timeframe for effect and what patients should expect. Treating anxiety with medications is not like treating ADHD, where there is an almost immediate robust response to a therapeutic dose. At the onset of treatment, parents and children should be told that these medications must be taken daily, will work better over time, and may take 2–3 weeks to show any effect and up to 6 weeks to show their full effects at a given dose. As long as there are no unbearable side effects, it is important to keep taking the medication consistently to see if a response is achieved and push through the doses. Despite the daunting nature of the list of possible side effects, most people tolerate SSRIs and serotonin-norepinephrine re-uptake inhibitors (SNRIs) very well. Table 11.3 provides a quick reference for information about SSRIs.

Please note that due to the relative dearth of studies regarding medication in children and adolescents compared to studies in adults, pediatric prescribing is often “off label.” While this is acceptable and often quite necessary, it must be explained to parents and patients ahead of time [17]. Of note, all antidepressants used in children and adolescents carry a black box warning from the FDA regarding suicidal thoughts and behaviors. Please refer to the Pharmacologic Interventions section of

Table 11.3 Non-SSRI medications for anxiety disorders [10, 18–24]

Medication	Medication class	Initial dose	Target dose	Maximum dose	Clinical considerations
Duloxetine (Cymbalta)	Serotonin and norepinephrine re-uptake inhibitor	20–30 mg per day	Children 40–60 mg Adolescents 40–60 mg	120 mg	FDA approved for generalized anxiety disorder for ages 7–17; also indicated for chronic pain and urinary continence; risk of elevated blood pressure; potential for drug-drug interaction via inhibition of CYP2D6; avoid use in hepatic disease
Venlafaxine XR (Effexor)	Serotonin and norepinephrine re-uptake inhibitor	37.5 mg	Children 150–225 mg Adolescents 150–225 mg	225 mg	FDA approved for generalized anxiety disorder from age 7 to 17. Acts as an SSRI at low dose; also indicated for chronic pain; use with caution with hepatic impairment. Can cause excessive sweating and tachycardia
Buspirone (Buspar)	Partial agonist of serotonin receptors	5 mg PO twice daily	15–60 mg/day divided BID	60 mg daily; consider lower dosing in younger children with lower body weight	No FDA approval for use in children and two RCTs in children w/ anxiety failed to detect effect; has one positive open-label study for social phobia; common side effects include dizziness, fatigue, drowsiness, nausea, headache, nervousness, xerostomia, and agitation

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Table 11.3 (continued)

Medication	Medication class	Initial dose	Target dose	Maximum dose	Clinical considerations
Hydroxyzine	Antihistamine	Start 5–25 mg PO BID to TID or weight-based dosing 2 mg/kg/day divided q6–8 h	May use weight-based dosing of 2 mg/kg/day divided PO q6–8 h	Maximum dose of 100 mg per day total. Consider smaller maximum dose for younger children with lower body weight	No FDA approval for treatment of anxiety in children; no RCTs for anxiety in children; may be used scheduled or as needed for acute anxiety. Common side effects include xerostomia, drowsiness, fatigue, ataxia, weakness, dysarthria, headache, and agitation. Note: younger children are more likely to have a paradoxical reaction to hydroxyzine

this text's Depression chapter as well as this text's Medicolegal Issues in Prescribing Medications to Children and Adolescents chapter for additional information when starting an antidepressant in a child, adolescent, or young adult for any reason. The Depression chapter includes a discussion of common antidepressant side effects, their associated black box warning regarding suicidal ideation, and Table 10.6, which includes talking points for parents about initiation of antidepressants.

Selective Serotonin Reuptake Inhibitors (SSRIs)

Due to their demonstrated efficacy in treating anxiety disorders and the fact that they are relatively well tolerated, SSRIs are the most widely used medications for anxiety disorders in children and adolescents. Common medication class side effects include headaches, nausea, vomiting, light-headedness, appetite changes, weight changes, sedation, palpitations, increased blood pressure, tremor, akathisia, sexual dysfunction, loose stool, and constipation. Monitoring for serotonin syndrome is indicated, especially when using higher doses and whenever there is polypharmacy.

Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)

Two of the medications in this class are FDA approved for anxiety disorders in children and adolescents; however, SNRIs may not be as effective or well tolerated for comorbid child and adolescent depression as fluoxetine, an SSRI medication [25]. Common class side effects include headaches, nausea, vomiting, light-headedness, appetite changes, weight changes, sedation, palpitations, increased blood pressure,

tremor, akathisia, sexual dysfunction, loose stool, and constipation. Monitoring for serotonin syndrome is indicated, especially when using higher doses and whenever there is polypharmacy.

Additional Medication Classes for Consideration

After first-line, FDA-approved treatments with relatively benign side effect profiles have been tried and have either not worked or caused intolerable side effects, alternative agents may be pursued. Note that the risk/benefit ratio and course of treatment necessitating these choices should be reviewed with families prior to their use.

Tricyclic antidepressants (TCAs) have plentiful studies supporting their use in anxiety disorders; however, overall they appear to be more effective in adults than in children and adolescents. They can be helpful for patients who have failed SSRIs and SNRIs. TCAs, however, are “dirtier” drug in that they tend to modulate receptors outside of serotonin and norepinephrine, such as anticholinergic receptors and histamine receptors. This can give them therapeutic advantages but also leaves them more prone to side effects, some of which are serious. TCAs used in children and adolescents include clomipramine, desipramine, and imipramine. Of note, TCAs can be fatal in overdose, which is an issue of clinical significance given the high rates of depression and anxiety comorbidity.

Benzodiazepines may interfere with learning, and they are also potential substances of abuse. Additionally, controlled trials do not support the use of benzodiazepines in children for anxiety [26, 27]. For these reasons, benzodiazepines are typically used either as short-term interventions for adjunctive treatment or for severe, functionally impairing anxiety symptoms. Compared to adults, adolescents are vulnerable to misusing benzodiazepines due to less well-developed executive functioning, decision-making, and impulse control. Also, the increased risk of death with the combination of benzodiazepines and other drugs of abuse, opiates in particular given the recent opioid epidemic, should be weighed prior to use. If there is a history of substance use/abuse in the patient, benzodiazepines should be avoided. Note that children, especially younger children, are more likely to have a paradoxical reaction to benzodiazepines. As with all drugs with the potential for abuse, formulations with faster onset and shorter duration of action can be more problematic.

When to Refer

Two primary factors determine when it is appropriate to refer the child or adolescent for additional treatment options. First, a referral is warranted when parental report indicates that the symptoms have created significant personal distress and impairment in the child’s functioning. This may be indicated by parental observation, teacher report, a decline in academic functioning, restricted social relationships, an increase in risky behavior, isolation, and other behaviors that are abnormal based on the caregiver’s typical observations. Second, subjective distress as noted by the

child or adolescent would indicate an additional reason to refer. Additionally, if initial interventions in the primary care setting do not yield an adequate treatment response, referral should be initiated.

Key Considerations for Follow-Up

Monitoring the effectiveness of treatment is an inexact science. As patients feel better, they generally report feeling calmer and less stressed. Additionally, at the time of diagnosis and treatment initiation, it is good to identify target symptoms to follow, such as somatic complaints, days of school achieved, number and severity of panic attacks in a given time span, improvement in sleep, or other markers that can be documented. As anxiety has likely kept patients from participating in their general interests and activities, a return to these exploits is seen as a great sign of progress. Rating scales can also be used at the beginning of treatment and along the course of treatment in order to measure the anxiety at baseline and its improvement as treatment moves forward. Short rating scales can be done in the waiting room prior to each appointment.

Determining whether the caregiver has followed recommendations for additional treatment is a key consideration when following up with the anxious child or adolescent. Considering there is a familial transmission of anxiety [1, 7, 8], inquiring as to whether the family has considered psychological and/or psychiatric treatment is essential due to the debilitating nature of avoidance behavior and functional impairment in the anxious family. Table 11.4 includes some key points for parental/family education about anxiety in children and adolescents.

Table 11.4 Key points for parental/family education

Key points for parental/family education
<i>Encourage families to combat avoidance behaviors and social withdrawal/isolation</i> —Permitting ongoing avoidance reinforces the problematic behavior creating more anxiety and distress long term. Supporting and facilitating gradual exposure to anxiety-provoking situations are key.
<i>Educate families on the importance of relaxation at bedtime</i> —Anyone who is not well rested will have more trouble handling stressful events, and trouble sleeping often comes with anxiety disorders. Every night before bed, breathing exercises (inhaling through the nose for 5 s and exhaling out the mouth for 6 s) coupled with anchoring (saying the five senses in the present moment) may be helpful. Additionally, consistent implementation of a calming bedtime routine is also valuable.
<i>Be on the lookout for declines in academic functioning</i> —Preoccupation with worried thoughts may make it difficult to concentrate or attend to instruction in school. If/when a youth does start to struggle academically, the associated distress and/or avoidance behaviors may make it difficult for the youth to bring up the issue. Monitoring of grades and communication with school personnel can provide accountability that will help combat avoidance behaviors as well as allow for earlier identification and addressing of problems.
<i>Address comorbid depressed mood, if present</i> —Explain the role of social support, and capitalize on existing prosocial and supportive relationships among family members and peers. Additionally, behavioral activation and pleasurable activity scheduling are great ways to elevate mood.
<i>Emphasize the importance of structure and consistency</i> —Having a routine and planning specific times to complete tasks can help a child feel more safe and secure.

Summary

Anxiety disorders in children and adolescents often first present in the primary care setting. Recognizing the symptoms early can lead to early interventions and decrease distress and impairment of function. Symptoms of anxiety can alter a child's cognitive, behavioral, and physical state and lead to avoidance behaviors that are then reinforced by the short-term relief from anxiety they provide. Addressing avoidance is a key aspect of psychosocial treatment. While psychotherapeutic and behavioral interventions are the first-line therapeutic modalities for addressing anxiety symptoms, psychopharmacology can be helpful and, when symptoms are severe, is indicated. Comorbid depression is common with anxiety disorders, and all youth with anxiety disorders should be screened for SUDs and trauma.

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