BAP GUIDELINES FOR THE MANAGEMENT OF

# Anxiety Disorders

1st Edition, 2022

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BANGLADESH ASSOCIATION OF PSYCHIATRISTS (BAP)

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Bangladesh Association of Psychiatrists (BAP)

**BAP Guidelines for the Management of Anxiety Disorders**



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**General Physicians**

General practitioners from different organizations took part in focus group discussions and shared their experience on the management of anxiety disorders.

**Patients/carers**

Patients and their carers took part in focus group discussions and shared their views.

**Focus Group Discussion Facilitators**

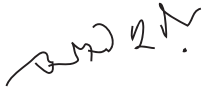
Dr. Md. Harun Ul Morshed and his team.

# Preface to the first edition

Anxiety disorders are the second most common type of mental illness in Bangladesh with a prevalence of 4.7% among adult persons. Their onset is usually in adolescence or early adulthood; the affected persons often develop further mental or physical illnesses and they are among the chronic illnesses with the greatest impact on patients' lives. Considering their prevalence and associated distress and disability, the Bangladesh Association of Psychiatrists (BAP) has felt the need to develop a management guideline for psychiatrists and for physicians working in other settings to improve clinical practice while recognizing, assessing, diagnosing and treating anxiety disorders.

This guideline is based on available evidence on epidemiology, diagnosis and treatment of anxiety disorders and obtained mainly through desk review of established guidelines. The suggestions in this guideline represent the view of BAP, arrived at after careful consideration of different evidence. However, we expect that the users will exercise their judgement, alongside with the individual needs, preferences and values of the patients. This guideline is intended to augment not replace sound clinical judgement.

I offer my special thanks and gratitude to Dr. M M Jalal Uddin, Convener, Working Committee; Dr. Mohammad Tariqul Alam, Coordinator of this guideline development project and Dr. Ahsan Aziz Sarkar for their immense contributions. I also extend my thanks to the experts who worked rigorously during this guideline development process. I believe this guideline will serve as a source of information for patients, their carers and health care professionals.



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We would like to express our gratitude towards the BAP members for their continued support and encouragement; the psychiatrists, general physicians, patients and their caregivers who participated in focus group discussions, gave their time and valuable feedback and the health care professionals involved in the management of anxiety disorders. A heartfelt thanks to Incepta Pharmaceuticals Ltd., scientific partner of this guideline development project for offering us logistical and financial support.

# CONTENTS

# Abbreviations

| | |
|---|---|
| BDZs | Benzodiazepines |
| CBT | Cognitive behavioral therapy |
| ECT | Electroconvulsive therapy |
| ERP | Exposure and response prevention |
| GAD | Generalized anxiety disorder |
| LFTs | Liver function tests |
| MAOI | Monoamine oxidase inhibitor |
| NaSSA | Noradrenergic and specific serotonergic antidepressants |
| NICE | National Institute for Health and Care Excellence |
| OCD | Obsessive compulsive disorder |
| PTSD | Post-traumatic stress disorder |
| RCT | Randomized controlled trial |
| SAD | Social anxiety disorder |
| SNRIs | Serotonin-norepinephrine reuptake Inhibitors |
| SSRIs | Selective serotonin reuptake inhibitors |
| SUD | Substance use disorder |
| TCAs | Tricyclic antidepressants |

# CHAPTER 1
# BACKGROUND

## 1.1 Introduction

Anxiety is a normal and necessary basic emotion required for survival. It can be a normal signal in the face of potential harm in presence of somatic illnesses (e.g., hypovolemia, hypoglycemia) or threats and dangers (e.g., snake, fire, academic examination).

Anxiety disorders are abnormal states in which there are mental and physical symptoms of anxiety, occurring in the absence of organic brain disease or another psychiatric disorder. In anxiety disorders the severity of anxiety is out of proportion to the threat or danger or it outlasts the threat.

Anxiety disorders are one of the most common groups of mental disorders. They are manifested as complex amalgamation of cognitive, affective, physiological and behavioral symptoms.

**Table 1: Symptoms of anxiety disorders**

| | |
|---|---|
| **Psychological** | Fearful anticipation<br>Irritability<br>Sensitivity to noise<br>Restlessness<br>Poor concentration<br>Worrying thoughts |
| **Autonomic** | **Gastrointestinal**<br>Dry mouth<br>Difficulty in swallowing<br>Epigastric discomfort<br>Excessive wind<br>Frequent or loose motions<br>**Respiratory**<br>Chest tightness/heaviness<br>Breathlessness<br>**Cardiovascular**<br>Palpitations<br>Discomfort in the chest<br>Awareness of missed beats<br>**Genitourinary**<br>Frequent or urgent micturition<br>Failure of erection<br>Menstrual discomfort |
| **Muscle tension** | Tremor<br>Headache<br>Aching muscles |
| **Hyperventilation** | Dizziness<br>Tingling in the extremities<br>Feeling of breathlessness |
| **Sleep disturbance** | Insomnia<br>Night terror |

**Chart reproduced from Shorter Oxford Textbook of Psychiatry, 7th ed., p. 162.*

Anxiety disorders involve dysfunction in brain circuits that respond to danger. An interaction between specific neurobiological vulnerability (genetic, childhood adversity) with environmental factors (stress, trauma) in susceptible individuals may trigger the disorders. In the central nervous system, the significant mediators of anxiety are thought to be norepinephrine, serotonin, gamma-aminobutyric acid (GABA), etc. The amygdala, limbic system and their connection with the prefrontal cortex showed abnormal activation in anxiety disorders.

In DSM-5, anxiety disorders include separation anxiety disorder, selective mutism, specific phobia, social anxiety disorder (SAD), panic disorder, agoraphobia, generalized anxiety disorders (GAD) and substance/medication induced anxiety disorder and anxiety disorder due to another medical condition. In this guideline we have discussed the management of specific phobia, social anxiety disorder, panic disorder, agoraphobia and generalized anxiety disorders.

## 1.2 Epidemiology

The National Mental Health Survey Bangladesh 2018-19 revealed that 4.7% adults are suffering from anxiety disorders; it is second most prevalent mental disorder in Bangladesh. Globally anxiety and related disorders' current prevalence ranges between 0.9% and 28.3%. Rates for individual disorders usually varies widely. Women generally have higher prevalence rates than men for most anxiety disorders.

Specific phobias are the most common anxiety disorders followed by social anxiety disorder (SAD), generalized anxiety disorder, panic disorder and agoraphobia. Generally, specific phobia starts during childhood, SAD during adolescence period, agoraphobia and panic disorder in third and GAD in fourth decades of life. Common risk factors for anxiety disorders are female gender, separated, divorced or widowed individual, less education or unemployment. Sociodemographic status may be considered as both a consequence and a cause of anxiety disorders.

A large number of patients with anxiety disorders visit general physicians, cardiologists, pulmonologists for the somatic symptoms of the disorders. Due to the high incidence of comorbid mental disorders, the course and prognosis also varies. Likelihood of anxiety disorders increases with the exposure to negative life events.

Anxiety and related disorders have a significant burden on patients and their family members as well as on society. With increasing severity of anxiety or comorbid anxiety disorders functional impairment substantially increases. Anxiety is associated with greater use of health care services and decreased work productivity. These disorders also tend to run a chronic course.

## 1.3 Rationale

Anxiety disorders are highly prevalent and distressing because of their early onset, severity and chronicity, and has negative impact on almost every aspect of a patient's life and well-being. Anxiety disorders are underrecognized and account for high morbidity. Anxiety disorders are the second leading mental health-related cause of disability-adjusted life-years (DALYs) and years lived with disability (YLDs) worldwide.

In Bangladesh, general physicians often come first in contact with these patients – evidence from focus group discussions suggest there is need for strengthening their skills. Although severe or chronic anxiety disorders need specialist psychiatric and psychological treatment, many of the less severe patients can be managed in primary settings. The overuse, underuse and misuse of drugs is a major problem worldwide and Bangladesh is not out of this irrational prescription trend. There is also no effective referral system at work in Bangladesh. Till date there is no single uniform management guideline for anxiety disorders in Bangladesh. Considering all these factors, Bangladesh Association of Psychiatrists (BAP) has felt the need to develop a national clinical management guideline for the psychiatrists and other physicians.

**BAP Guidelines for the Management of Anxiety Disorders**


**Features of this guideline:**

1. Diagnosis and management can be carried out by psychiatrists as well as other physicians working in low resource settings.

2. The concepts, assessment, management and referral pathways are clearly described here.

3. The clinical features, different types and special population with anxiety disorders (child and adolescent, pregnant and lactating mother, elderly, people with physical comorbidity, etc.) are considered in this guideline.

4. A nationwide service mapping for management of anxiety disorders is included here which will serve as a basis for rational liaison psychiatric service.

5. The evidence-based principle of management has been developed here after considering country context, cultural compatibility and available resources.

6. This guideline comprises information to be used in inpatient, outpatient, emergency hospital and clinic settings as well as private practice.

7. A comprehensive management plan including follow up and compliance issues are also discussed here.

8. This guideline will be updated periodically.

All these things have made this guideline unique and uniform and very much compatible with Bangladesh context.

## 1.4 Objectives

a. To provide clear, concise and uniform information to all psychiatrists and other physicians on the current concept in the management of anxiety disorders considering the context of Bangladesh.

b. To provide necessary directives and primary management algorithm along with the referral pathways for the physicians working in non-specialized settings.

c. To develop a user-friendly guideline to ensure advance and updated management of different anxiety disorders as well as primary care model for physicians working in non-specialized settings.

## 1.5 Target users and their roles

| | |
|---|---|
| Psychiatrists | • Advanced and updated management protocol for clinical practice<br>• Covers all aspects of management of common anxiety disorders<br>• Management in special population and situations |
| Physicians working in non-specialized settings | • Primary management protocol [what to do and what not to do]<br>• Referral pathway [when to refer, where to refer, how to refer] |

# CHAPTER 2
# METHODOLOGY

# 2 Methodology

**Table 2: Definition of levels of evidence criteria used in this guideline**

| Level | Evidence | BAP evidence gathering |
|---|---|---|
| i | Systematic review/meta-analysis of all relevant randomized controlled trials | Obtained from desk review |
| ii | One or more properly designed randomized controlled trial | |
| iii | Well-designed prospective trial (non-randomized controlled trial); comparative studies with concurrent controls and allocation not randomized; case-controlled or interrupted time series with a control group | |
| iv | Case series, either post-test or pretest/post-test | |
| v | Expert opinion | Consensus among experts, focus group discussion with experts |

This guideline has been developed after desk review of established guidelines and literature, focus group discussions with the psychiatrists, general practitioners and persons with living experience of anxiety disorders in Bangladesh and expert opinion of senior psychiatrists. For desk review we consulted updated clinical practice guidelines from several authorities like American Psychiatric Association (APA), National Institute for Health and Care Excellence (NICE), British Association of Psychopharmacology (BAP), The Royal Australian and New Zealand College of Psychiatrists (RANZCP), Canadian Network for Mood and Anxiety Treatments (CANMAT), The World Federation of Societies of Biological Psychiatry (WFSBP), Indian Psychiatric Society (IPS), etc.

Hierarchical ranking of treatment recommendations is used in this guideline. They were created by considering the efficacy of each treatment modalities across various states of illness as well as safety and tolerability obtained from levels of evidence from various types of studies. We recommend that drugs listed top in the hierarchy be tried first, unless there are patient specific reasons for choosing a drug lower in the hierarchy.

# CHAPTER 3
# GENERAL MANAGEMENT PLAN

# 3.1 Management principles of anxiety disorders

Management principles of anxiety disorders

The management of persons suffering from anxiety disorders includes five main components of management.

**Box 1: Components of management of anxiety disorders**


**a. Assessment**

Assessment starts with the history of having any psychological symptoms of anxiety such as excessive anxiety, worry, fear, avoidance behavior, intrusive thoughts and physical symptoms such as restlessness, palpitation, nonspecific body pain, fatigue, muscle tension, etc. which is well outlined in DSM-5 criteria of anxiety disorders. Mental State Examination (MSE) and different screening questionnaire for anxiety disorders are also helpful.

**b. Formulation**

During assessment possible differential diagnoses like medical or psychiatric conditions (hyperthyroidism, cardiopulmonary disorder, traumatic brain injury, etc.) or drugs (thyroxine, antihypertensives, bronchodilators, anticholinergics, antiarrhythmics and NSAIDS, etc.) responsible for such anxiety symptoms need to be considered. Family or personal history of anxiety or mood disorders, and stressful live events are strong predictor of anxiety symptoms.

More than half of the patients have more than one type of anxiety disorders and almost 30% have at least three or more co-morbid anxiety disorder. Other co-morbid psychiatric disorders are bipolar mood disorder, major depressive disorder, obsessive compulsive disorder and substance related disorders. Patients with anxiety disorders have high prevalence of hypertension, cardiovascular disease, arthritis, thyroid disease, respiratory disease, migraine headache and allergic conditions.

**c. Diagnosis**

Identification of specific anxiety disorders should be done by taking detailed history, mental state examination, physical and biochemical assessment using DSM-5 criteria of anxiety disorders. Table 15 in annexure gives a glimpse of main symptoms observed in different anxiety disorders; see the glossary part for detail diagnostic criteria.

**d. Treatment**

Treatment options for anxiety disorders include pharmacological and psychological treatments. Patients should receive education about their disorder, available treatment options, efficacy and tolerability of treatment choices, triggering factors and signs of relapse.

The choice of pharmacological and psychological treatment depends on factors such as patient preference and motivation, compliance of treatment, severity of illness, availability of treatments, patient's prior treatment response and/or the presence of comorbid medical or psychiatric disorders and personal, family and cultural attitude toward illness.

Anxiety disorders can be treated on an outpatient basis but may require hospitalization if there is suicidality, unresponsiveness to standard treatments, or relevant comorbidity, e.g., with major depression, personality disorders, or substance abuse.

**e. Follow-up**

Anxiety and related disorders are usually chronic in course and needs regular follow-up. Usually, it takes 4-6 weeks for symptomatic remission for anxiety symptom in case of pharmacological treatment and longer duration is needed for psychological treatment. Regular monitoring of side effects of medications with physical and biochemical monitoring is essential. Regular follow-up for psychological treatment is also recommended.

Anxiety disorders should ideally be managed by psychiatrists. However, general physicians and specialists from other disciplines are usually the first point of contact with these patients. For the wellbeing and proper management of the patients, they must refer to a psychiatrist in cases when

1. The anxiety symptoms are chronic, severe and disabling.
2. The patient is elderly, pregnant or is a child or adolescent.
3. The diagnosis is uncertain.
4. Comorbid illicit drug use is present.
5. Comorbid medical or mental illness is present (e.g., heart disease, diabetes, depression).
6. There is risk of suicide or self-harm.
7. Persons who cannot get to work or maintain usual activities.
8. Poor response to standard treatment. The response should be evaluated within a period of 6-8 weeks.

The main difficulty in referring to psychiatric services is stigma attached to it and in few cases unavailability of the service. As a consequence, referral needs to be handled tactfully. For routine referral, a period of standard first-line drug trial evaluation period (6-8 weeks) is reasonable. However, in many cases, urgent referral (within the same day) may be needed.

## 3.2 Overview of drugs

Advantage of pharmacotherapy in management of anxiety disorders is its efficacy, quick onset of action, availability, lower cost and suitable for use in primary care. Antidepressants especially SSRIs and to lesser extent SNRIs are the first line medications for anxiety disorders especially for panic disorder, GAD and SAD. There are very few studies on drug treatment for specific phobias.

TCAs and MAOIs have demonstrated some efficacy in treatment of anxiety disorder but SSRI is preferred due to their tolerability and side-effects profile. Benzodiazepines may be useful as adjunctive treatment in anxiety disorders especially in panic disorder and in acute conditions of anxiety states. Benzodiazepines should only be used for short-term due to its abuse potential and dependence.

Several anticonvulsants and atypical antipsychotics have demonstrated efficacy in some anxiety disorders but due to limited evidence in RCT, tolerability and side-effects these agents are generally recommended as second-line, third-line, or adjunctive therapy. They should be used only under psychiatrists' supervision. Overall pharmacological treatment recommendations for anxiety disorders in adults are given in annexure (table 16). Specific recommendations are given under specific disorder.

**General treatment principles**

1. Drug treatment needs be considered as the initial treatment choice for different anxiety disorders followed by different types of psychotherapy when available. Combination of pharmacotherapy and psychotherapy works better.

2. Choose one of the first-line drugs considering safety, tolerability, pharmacokinetic and pharmacodynamic issues for the individual patient.

3. Patients must be informed about the efficacy, adverse effects, serious adverse effects, usual duration of onset of action of the prescribed drugs.

4. In three-fourths of the cases of anxiety disorders, doses in the lower part of the therapeutic range are sufficient.

5. Onset of anxiolytic effect of antidepressants usually takes 2 to 4 weeks (in some cases up to 6 weeks). During the initial weeks side effects may be stronger. Lowering the starting dose may reduce adverse effect.

6. Careful consideration of factors related to course and prognosis for individual patient will determine how long the drug therapy should be continued after remission. Usual recommendation is - drug treatment should be continued for 6 months or longer depending on the type of anxiety disorder.

7. To avoid withdrawal symptoms, dose should be gradually tapered off over a period of 2 to 4 weeks.

8. Benzodiazepines are used for quick relief of anxiety symptoms.

9. For anxiety disorders, benzodiazepines should be tapered off after 2-4 weeks given their abuse potential, tendency to cause dependence and cognitive impairment. They should be avoided in patients with history of substance use (including benzodiazepine abuse).

10. In case of non-response diagnosis should be reviewed, adherence checked, drug interaction and metabolism considered, dose optimized (or highest tolerable dose) and need to make sure the trial period was of adequate duration.

11. Psychotherapy if available can be added at any steps of the drug treatment.

One general rule is that in case of partial response either optimize the dose or add an adjunctive drug with the ongoing treatment. In case of non-response switch to another drug indicated for the treatment of anxiety disorder. When initial treatment is ineffective, Table 3 provides a guide for management of anxiety disorders. For details look at the management of specific disorder section.

**Table 3: Stepwise plan for drug treatment if the initial standard drug treatment was ineffective or poorly tolerated**

| | | |
|---|---|---|
| **Step 1** | | |
| Switch from one standard drug to another | | Switch from one SSRI to another SSRI<br>Switch from an SSRI to an SNRI, or vice versa<br>Switch to a TCA<br>Switch to Pregabalin (only in GAD) |
| **Step 2** | | |
| Switch to a drug that is approved for other anxiety disorders | | Switch to *Moclobemide, Opipramol,*or Hydroxyzine<br>Add Benzodiazepine |
| **Step 3** | | |
| Switch to a drug that is not approved for the anxiety disorder in question but has been found effective in RCTs | PDA<br>GAD<br>SAD | Mirtazapine, Quetiapine, *Phenelzine*<br>Quetiapine, Agomelatine<br>Mirtazapine, Gabapentin, Pregabalin, Olanzapine |
| **Step 4** | | |
| Switch to a drug (or drug combination) that has been found effective in open studies | PDA<br><br><br><br><br><br><br><br>GAD<br>SAD | SSRI + TCA<br>Olanzapine monotherapy<br>SSRI + Olanzapine<br>SSRI + Pindolol<br>Valproate+ Clonazepam<br>Fluoxetine + TCA + Olanzapine in refractory cases<br>Ziprasidone<br>Levetiracetam, Topiramate,<br>SSRI + Buspirone |

*PDA, panic disorder with agoraphobia; GAD, generalized anxiety disorder; SAD, social anxiety disorder; Italics are not available in Bangladesh market*

*Note: From - Bandelow B, Zohar J, Hollander E, et al. World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the pharmacological treatment of anxiety, obsessive-compulsive and post-traumatic stress disorders – first revision. World J Biol Psychiatry. 2008;9(4):248-312.*

## 3.3 Laboratory investigations

Ideally, with physical examination the baseline laboratory investigations should be performed before pharmacotherapy is initiated. Box 2 shows some of the commonly performed laboratory investigations. Specific tests should be chosen on the basis of careful clinical deliberation for individual patient.

**Box 2: Considerations for baseline laboratory investigations (as needed based on patient's presenting symptoms)**

**Basic lab tests**

- Complete blood count
- Random blood glucose
- Thyroid stimulating hormone (TSH)
- Fasting lipid profile
- Liver enzymes (SGPT, Alkaline Phosphatase)
- Electrolytes
- ECG
- Chest X-Ray

**If warranted**

- Urine toxicology for substance use
- EEG
- Echocardiography

## 3.4 Non-pharmacological management of anxiety disorders

Decisions about providing psychological treatment should be made after considering the severity of the disorder, the preference of the informed patient, the durability of the treatment effect and the availability of the treatment in question. Considering the context of Bangladesh, where psychological treatment opportunities are less available outside the capital, we recommend to use pharmacological treatment options as first-line approach.

Several meta-analyses have reported that psychotherapy is usually effective in case of mild, transient symptoms and when anxiety disorders are without associated impairment in social and occupational function. In more severe cases, there is scarce evidence for the efficacy of psychotherapy. Few experts recommend combining drug treatment with psychotherapy for longer-lasting effect (e.g., for specific phobia and SAD).

**Table 4: Outlining main characteristics of advice, counselling and psychotherapy**

| | Advice | Counselling | Psychotherapy |
|---|---|---|---|
| **Overview** | A relevant piece of information provided by a health professional to resolve a problem or overcome from difficulty | Professional advice given by a counselor to an individual to help him overcome personal or psychological problems | Established structured psychological treatment that require a specific and elaborate training |
| **Aim** | Provide reassurance and support | A clear set of instructions with underlying theoretical principles which focuses on specific problem and changing behavior of patient | Explore the cause of the current problems and try to change the personality, cognition, etc. of the patient |
| **Who can provide it?** | Physician from any discipline (non-mental health professional) | Mental health professionals | Psychiatrists and clinical psychologists |

All patients with anxiety disorders should receive psychoeducation. Involvement of spouse and family members are needed in many cases. Essential elements of psychoeducation are listed in Box 3. Psychotherapy when needed should be provided by registered mental health professionals. Table 5 lists the effective psychotherapies for anxiety disorders.

For children, pregnant women and older adults with anxiety disorders psychotherapy is recommended by some experts. Given the limited availability of psychotherapy in Bangladesh – decision should be made on individual patient basis along with the consideration of the severity of the disorder and impact on patient and fetal life.

**Box 3: Essential components of psychoeducation for anxiety disorders**

- Etiological factors
- Common signs and symptoms
- Awareness regarding the early signs of relapse/recurrence
- How to cope with the situation
- Various treatment options available
- When and how to seek treatment
- Need for adherence to treatment as per the guidance of treating team
- Long-term course and outcome
- Dos and don'ts for family members while dealing with the patient
- Clearing myths and misconceptions about the illness and dispelling stigma
- Relationship between personality traits and vulnerability to anxiety

**Table 5: Suggested psychotherapies for anxiety disorders**

| Disorder | Therapy |
|---|---|
| Specific phobia | Behavioral therapy (exposure therapy)<br>Cognitive behavioral therapy (CBT) |
| Social anxiety disorder | Cognitive behavioral therapy (CBT) |
| Panic disorder | Cognitive behavioral therapy (CBT) |
| Agoraphobia | Cognitive behavioral therapy (CBT) |
| Generalized anxiety disorder | Cognitive behavioral therapy (CBT) |

For patients with anxiety symptoms but not anxiety disorders guided self-help (e.g., written materials from BAP), psychoeducational group might be useful. Some non-specific techniques can be useful in controlling anxiety symptoms; however, in cases of anxiety disorders, alone they are not effective. For anxiety disorders, these techniques need to be incorporated with the psychotherapy.

**Box 4: Other non-pharmacological interventions used to control anxiety symptoms**

Breathing exercise

Relaxation with imagery

Progressive muscular relaxation

Problem solving therapy

Mindfulness

Coping skills development

Stress management

Social skills training

Physical activity and exercise

Healthy lifestyle

# CHAPTER 4
# TREATMENT OF ANXIETY DISORDERS

## 4.1 Specific phobia

Specific phobia is a strong and inappropriate fear of a particular object or situations and usually associated with avoidance. Five general types of specific phobia are recognized-

- Animal (e.g., spiders, insects, dogs).
- Natural environment (e.g., heights, storms, water).
- Blood-injection-injury (e.g., needles, invasive medical procedures).
- Situational (e.g., airplanes, elevators, enclosed places).
- Other (e.g., situations that may lead to choking or vomiting; in children e.g., loud sounds or costumed characters).

### Epidemiology

Estimated lifetime prevalence of specific phobia is 10-13% and a 12-month prevalence is 7-9%. Specific phobia is more common in females than in males. The age of onset usually ranges from 5 to 12 years.

Animals and blood-injection-injury phobias generally begin in childhood, situational phobia (e.g., driving a car, claustrophobia) appear late, typically in late adolescence or early adulthood.

### Comorbidities

Specific phobias tend to occur with other specific phobias with less than 10% of patients having only one fear. On average individual with specific phobia fears three objects or situations and about 75% of individuals with specific phobia fear more than one situation or object. In addition, specific phobias often co-exist with other mental disorders, including substance use disorders, mood disorders, and other anxiety or related disorders (especially panic disorder, SAD, and GAD) and personality disorders.

### Differential diagnosis

OCD, illness anxiety disorder, panic disorder.

**Treatment**

Exposure therapy is the mainstay of treatment for specific phobia (see table 17 in annexure for more detail form of exposure therapy used). Few sessions are usually required. Pharmacological treatments have minimal effect.

**Table 6: Pharmacological treatment for specific phobia**

| Indication | Drug |
|---|---|
| All specific phobias<br>To relieve acute symptoms while facing a feared situation (e.g., dental procedure, magnetic resonance imaging [MRI], unexpected flight) | SSRIs<br>Benzodiazepines (e.g., lorazepam, clonazepam) |

## 4.2 Social anxiety disorder (SAD)

Social anxiety disorder (SAD) or social phobia is the persistent fear of or anxiety about one or more social or performance situations that is not at normal level. Typical situations that provoke anxiety may include starting conversations, talking with strangers, authority figures, in groups and meetings, eating in restaurants, going shopping, using public places, public performances such as public speaking, etc. Children may avoid interactions, cry, freeze or have tantrums in similar situations.

### Epidemiology

Social anxiety disorder (SAD) is one of the most common anxiety disorders. Its prevalence (8-12%) is higher in comparison to other anxiety disorders and it typically begins in early adolescence.

### Comorbidities

Common comorbidities of SAD include depression, substance abuse, generalized anxiety disorder, panic disorder, PTSD, OCD, avoidant personality disorder, etc.

### Differential diagnosis

To confirm SAD, common differential diagnoses like normal shyness, other anxiety disorders, avoidant personality disorder, body dysmorphia, autism, oppositional defiant disorder, etc. need to be excluded.

### Treatment

- Cognitive behavioral therapy (CBT) designed for SAD should be the first choice of treatment.
- An SSRI (e.g., sertraline, escitalopram) is the first choice if the person prefers, do not interested in taking CBT, if CBT is not available or has more severe symptoms.
- In case of partial or no response to CBT, consider prescribing an SSRI.
- If there is no or partial response after 12 weeks of optimum dose of SSRI treatment, combine SSRI with CBT.

#### a. Psychological treatment

Cognitive behavioral therapy (CBT) designed for SAD should be used. Individual CBT is associated with better treatment outcomes than group CBT.

#### b. Pharmacological treatment

- If there is no response to a first-line drug (after 12 weeks of sole pharmacotherapy) or the person can't tolerate it due to side effects, use a second-line drug.
- Prescribe a third-line drug when there is no or partial response to a second line drug.

- Benzodiazepines have proven efficacy in the treatment of SAD. Cognitive impairment, drowsiness, sedation, tolerance and dependence are troublesome side effects and should only be used for short term control of anxiety symptoms.
- Beta-blockers can be successfully used in performance anxiety.
- Continue any drug treatment for 12 weeks to assess efficacy.
- Continue same drug treatment for at least six (6) months in a patient who has responded to a treatment.
- Do not routinely offer pharmacotherapy to treat SAD in children.
- Routine prescription of higher dosage of SSRI is not recommended.
- Benzodiazepines or beta-blockers should not be used as main or sole treatments.

**Table 7: Pharmacotherapy for social anxiety disorder**

| | |
|---|---|
| First-line | Sertraline<br>Escitalopram |
| Second-line | Fluoxetine<br>Fluvoxamine<br>Paroxetine<br>Venlafaxine |
| Third-line | *Phenelzine*<br>*Moclobemide* |
| Others | Benzodiazepine (clonazepam, bromazepam)<br>Beta-blockers (atenolol, propranolol)<br>Pregabalin<br>Olanzapine<br>Buspirone |

*Italics are not available in Bangladesh*

**When there is initial treatment failure**

Review the diagnosis and check for comorbidities.

Step 1 - Combine SSRI with CBT.

Step 2 - Increase dose of SSRI in well tolerated patients (in selected cases only, switching appears more efficacious than raising dosage).

Step 3 - Switch to a second-line drug.

Step 4 - Augment with benzodiazepine, pregabalin, olanzapine, buspirone, etc.

Step 5 - Consider referral to a tertiary or specialized hospitals.

## 4.3 Panic disorder

Panic disorder is characterized by recurrent panic attacks with discrete periods of intense fear or discomfort, anticipatory anxiety, accompanied by severe autonomic activity, palpitations, sweating, dyspnea, choking sensation or other somatic symptoms like chest pain, trembling, nausea, discomfort, fluttering sensation in abdomen, impending fear of death, etc. Patient perceives it as a serious medical condition and often worry about additional attacks or consequences. A panic attack starts abruptly, reaches a peak within 10 minutes and lasts for 30 – 45 minutes on average.

### Epidemiology

The lifetime and 12-month prevalence of panic disorder have been estimated at 4.7-5.1% and 2.1-2.8%, respectively. The risk of panic disorder is higher in women than men, and patients who are middle-aged, widowed/divorced, and those of low income.

### Comorbidities

Panic disorder frequently co-occurs with agoraphobia. Other psychiatric comorbidities include other anxiety disorders, mood disorder, impulse-control disorder, substance abuse, PTSD, etc. Medical comorbidities might include thyroid disease, hypoglycemia, chronic pain, cardiac disease, etc. Panic attacks may also be associated with intoxication or withdrawal from drugs of abuse, medications such as decongestants, stimulants, or beta-adrenergic agonist inhalers, or caffeine.

### Differential diagnosis

Other anxiety disorders, angina, asthma, congestive heart failure, mitral valve prolapse, pulmonary embolism, substance use disorder, etc.

### Treatment

Pharmacotherapy or psychotherapy or combination of both are used in the treatment of panic disorder. A combination of CBT and medication offers best treatment outcomes. Following forms of psychotherapy are usually considered in panic disorder -

- Cognitive behavioral therapy
- Behavioral techniques (BT) (e.g., graded exposure)

Before starting any medication, psychoeducation should be provided about anxiety and panic symptoms, and advice given about lifestyle factors that may be contributing or perpetuating symptoms. Potential adverse effects of medication should also be discussed carefully.

**Table 8: Pharmacotherapy for panic disorder**

| | |
|---|---|
| First-line | SSRIs (Citalopram, Escitalopram, Fluoxetine Fluvoxamine, Paroxetine, Sertraline) |
| Second-line | Imipramine<br>Clomipramine<br>Mirtazapine |
| Third-line | *Phenelzine*<br>*Moclobemide*<br>Atypical antipsychotics (e.g., low dose Quetiapine, Risperidone) |
| Others | Benzodiazepine (Clonazepam, Diazepam, Alprazolam, Lorazepam)<br>Beta-blockers (Propranolol, Atenolol) |

*Italics are not available in Bangladesh*

To assess the efficacy of pharmacotherapy, treatment should be continued for at least 12 weeks with at least two weeks at the maximum tolerable dose. Usually, the treatment is stopped in a tapering manner after at least 6 months' stability of clinical improvement and asymptomatic status of the patient.

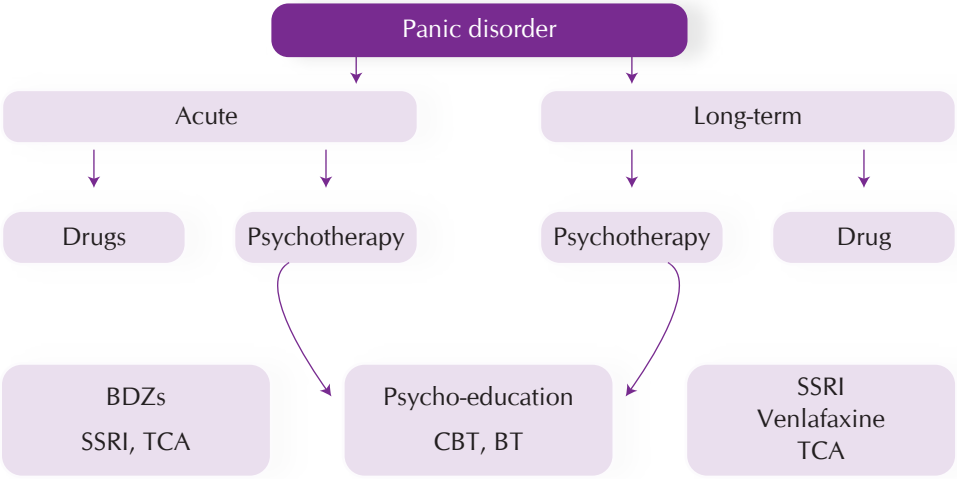


**Figure 1: Treatment algorithm for panic disorder**

## 4.4 Agoraphobia

Agoraphobia is an anxiety disorder that occurs when one is in a public or crowded place, from which a potential escape may be difficult, or help may not be readily available. It is characterized by the fear that a panic attack or panic-like symptoms may occur in these situations. Individuals with agoraphobia, therefore, try to avoid such situations or locations. The most important feature is marked, or intense, fear or anxiety nearly every time a person is exposed to at least two of the following five situations:

- Using public transportation, such as automobiles, buses, trains, ships, or planes
- Being in open spaces, such as parking lots, marketplaces, or bridges
- Being in enclosed spaces, such as shops, theaters, or cinemas
- Standing in line or being in a crowd
- Being outside of the home alone

### Epidemiology

The lifetime prevalence of agoraphobia varies from 2 to 6% across studies. It is two to three times more common in women than men. It may occur in childhood, but incidence peaks in late adolescence and early adulthood.

### Comorbidities

Common comorbid disorders are panic disorder, specific phobia, social anxiety disorder, major depressive disorder, PTSD, and substance use disorder. Common medical comorbidities include thyroid disease, cardiac disease, respiratory conditions, etc.

### Differential diagnosis

Agoraphobia may be confused with other anxiety disorders, such as social phobia, GAD, Panic disorder, separation anxiety disorder, depressive disorder, PTSD; delusional disorder sometimes may mimic agoraphobia.

**Treatment**

Exposure-based cognitive behavioral therapy (CBT) is the preferred treatment in agoraphobia. SSRIs, SNRIs and CBT demonstrate good efficacy with moderate-to-large effects on agoraphobia. Particularly for agoraphobia/panic disorder, available data further point to a synergistic effect of second-generation antidepressants and CBT.

**Table 9: Pharmacological treatment for agoraphobia**

| | |
|---|---|
| First-line | SSRIs (Fluoxetine, Sertraline, Paroxetine, Citalopram)<br>SNRIs (Venlafaxine) |
| Second-line | Imipramine, Clomipramine |
| Third-line | Atypical antipsychotics (e.g., low dose Quetiapine, Olanzapine, Risperidone) |
| Others | Benzodiazepine (Clonazepam, Diazepam, Alprazolam, Lorazepam) |


**Figure 2: Algorithm of management of agoraphobia**

## 4.5 Generalized anxiety disorder (GAD)

Generalized anxiety disorder is characterized by persistent, excessive, and unrealistic worry about everyday things. This worry could be multifocal such as finance, family, health, and the future. It is excessive, difficult to control, and is often accompanied by many non-specific psychological and physical symptoms. Apart from worry other common symptoms include restlessness, feeling keyed up or on edge, being easily fatigued, difficulty in concentrating or mind going blank, irritability, muscle tension, sleep disturbance, irritability, etc.

### Epidemiology

GAD is a common condition and estimated 1-year prevalence ranges from 2 to 5%. The ratio of women to men is about 2 to 1 and it has its onset in early or late adulthood.

### Comorbidities

Common comorbidities include other anxiety disorders, depressive disorders and substance use disorders.

### Differential diagnosis

Differential diagnoses include other anxiety disorders, depressive disorders, PTSD, OCD, etc. Medical comorbidities may include hyperthyroidism, pheochromocytoma, chronic obstructive pulmonary disease (COPD), transient ischemic attack (TIA), epilepsy, use of caffeine and decongestants may mimic presentation of GAD.

### Treatment

The two main treatments for generalized anxiety disorder are cognitive behavioral therapy and medications. Patients may benefit most from a combination of the two. Pharmacological interventions are effective in treating GAD. There is strong evidence for SSRIs, SNRIs, TCAs, benzodiazepines, pregabalin, quetiapine XR, and several other agents. Adjunctive therapy is recommended in case of inadequate response to repeated trials with first-line or second-line agents. As an adjunctive therapy agent pregabalin, low doses of risperidone, olanzapine, quetiapine XR and aripiprazole have shown some efficacy in GAD.

**Table 10: Pharmacological treatment for generalized anxiety disorder**

| | |
|---|---|
| First-line | SSRIs (Sertraline, Paroxetine, Escitalopram)<br>SNRIs (Venlafaxine, Duloxetine)<br>Pregabalin<br>Agomelatine<br>Buspirone |
| Second-line | Quetiapine extended release, Imipramine<br>Hydroxyzine |
| Third-line | Citalopram, Fluoxetine, Mirtazapine<br>Valproate |
| Others | Benzodiazepine (Clonazepam, Diazepam<br>Alprazolam, Lorazepam) |

# COMORBIDITIES

# 4.6 Psychiatric Comorbidities

### Depression

- Major depression is a common psychiatric comorbidity of anxiety disorders and is associated with greater impairment, more hospitalization and more symptom intensity. When present, always assess for suicide and self-harm risks.
- Pharmacotherapy for anxiety disorders also works for depression. An SSRI (citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine or sertraline) that the patient had responded to or will be used for anxiety disorders should be prescribed.
- An SSRI + Lithium or an SNRI (venlafaxine, duloxetine) could be tried in case of non-response to initial therapy.
- Severe depression with high suicidal intent needs thorough evaluation.
- Cognitive behavior therapy (CBT)

### Substance use disorder

- Research indicates that a great number of patients with anxiety disorders abuse various kinds of substances specially sedatives and alcohol. Substances can trigger or worsen anxiety symptoms during their administration or withdrawal.
- Prioritizing treatment of the substance abuse is necessary, as well as integrated treatment of the anxiety disorder and substance use.
- Combined CBT and SSRI treatment significantly reduce anxiety symptoms and alcohol dependence.
- Benzodiazepines should be carefully use in patients with history of substance abuse as dependence may develop.
- If drug therapy is indicated, SSRIs or SNRIs are preferred above TCAs.

### Another anxiety disorder

- Up to one-third patients with one anxiety disorder have another comorbid anxiety disorder.
- Treatment with SSRIs, SNRIs, or CBT is appropriate for most patients with comorbid anxiety disorders. Treatment for one disorder often have a positive effect on symptoms of another disorder.
- When available, highly tailored CBT directed at both disorders can be used.

### Personality disorder

- It is estimated that 40–50% of patients with anxiety disorders meet the criteria for one or more personality disorders, most common being avoidant, obsessive-compulsive and dependent personality disorders.
- Co-occurring personality disorder presents with more severe anxiety symptoms, greater chronicity and relapse and associated with poorer response to standard treatment.
- When present, strengthening therapeutic alliance is important and con-current psychological management of personality disorder is necessary.

**Table 11: Recommended management for comorbid psychiatric disorders in anxiety disorders**

| | |
|---|---|
| Depression | Pharmacotherapy for anxiety disorders also works for depression |
| Substance use disorder | SSRI + CBT<br>SNRI + CBT |
| Another anxiety disorder | Pharmacotherapy for one anxiety disorder works for another<br>Tailored CBT for both conditions |
| Personality disorder | Psychological treatment |

# 4.7 Medical Comorbidities

## Chronic painful conditions

- Depression and anxiety symptoms may develop in chronic painful conditions or chronic pain can be a manifestation of depression and anxiety states. Up to one-third to half of the patients with chronic painful conditions show depressive and anxiety symptoms.
- Appropriate pain control strategies should be adopted before targeting anxiety symptoms.
- CBT with relaxation techniques appear effective in many instances.
- SNRIs (duloxetine, venlafaxine), SSRIs (fluoxetine, paroxetine, sertraline) and pregabalin showed efficacy both in controlling anxiety symptoms and reducing noncancer chronic painful conditions like musculoskeletal pain associated with osteoarthritis and chronic low back pain.

## Hepatic impairment

General guideline for prescribing in hepatic impairment

- Use lower starting doses.
- Be cautious with drugs that are extensively metabolized in liver.
- Avoid drugs with long half-lives, that are very sedative and very constipating.
- Treat with a single drug whenever possible.
- Choose a low-risk drug and initially (first six weeks) monitor liver function tests weekly.
- CBT appeared effective in patients with hepatic impairment

| Box 5: Recommended medications in hepatic impairment |
|---|
| **SSRIs** – Sertraline (first-line); Escitalopram, Fluvoxamine and Paroxetine (second-line) |
| **Pregabalin** |

Note:
Sertraline, escitalopram, fluvoxamine, paroxetine - Start at half of the recommended dosage in mild to moderate impairment; maximum dose may be half of usual maximum dose.

Severe impairment - more caution required (e.g., 75% dose reduction).

### Renal impairment

General guideline for prescribing in renal impairment

- Avoid drugs that are extensively renally cleared.
- Start at a low dose, increase gradually
- Use Creatinine clearance and ACR (albumin creatinine ratio) to decide about dose range and titration frequency.
- Usual dosing: GFR 10-50ml/min - use normal dose; GFR < 10ml/min – use1/4 to 1/2 of normal dose.
- If drug treatment is necessary, sertraline and citalopram are the preferred choices in patients with renal impairment.

### Cardiovascular disease

- Cardiovascular adverse events are usually mild and are unlikely to occur with SSRIs at therapeutic doses. All SSRIs appear safe at therapeutic doses.
- Orthostatic hypotension, mild bradycardia and QT interval prolongation have been reported under SSRIs and usually in those cases patients had preexisting conditions like long QT syndrome, recent myocardial infarction, hypokalemia, hypomagnesemia, etc. Also, SSRIs interacts with warfarin and other anticoagulants.
- SSRIs may have antithrombotic cardioprotective properties through blocking the serotonin reuptake during platelet aggregation.
- If drug treatment is necessary, sertraline and fluoxetine are the preferred choices in patients of anxiety disorders with heart disease.

**Table 12: Recommended drugs for anxiety disorders with comorbid medical conditions**

| | |
|---|---|
| Chronic pain | Appropriate pain control<br>SNRIs (Duloxetine, Venlafaxine)<br>SSRIs (Fluoxetine, Paroxetine, Sertraline)<br>Pregabalin |
| Hepatic impairment | SSRIs – Sertraline (first-line); Escitalopram,<br>Fluvoxamine and Paroxetine (second-line)<br>Pregabalin |
| Renal impairment | SSRIs - Sertraline, Citalopram |
| Cardiovascular disease | SSRIs - Sertraline, Fluoxetine |

# SPECIAL POPULATION

# 4.8 Special population

### Children and adolescents

- Most patients suffering from anxiety disorders have their illness onset during childhood or adolescent period. They can be significantly disabled by persistent, distressing and severe anxiety symptoms.
- CBT adapted for children and adolescents with anxiety disorders is the treatment of choice. It is important to engage parents in the treatment process.
- In children, SSRIs (fluoxetine, sertraline or fluvoxamine) should be the preferred choice of treatment when CBT facilities are not available or when the patient is unresponsive to CBT.
- An adequate trial of medication (SSRI) should be continued for at least 12 weeks. Most patients show gradual improvement over several weeks.
- At the beginning of treatment with SSRIs, careful monitoring is required for possible appearance of suicidal behavior, self-harm or hostility.
- Medication should be continued for at least 6 months post remission.
- Dose should be tapered gradually over several weeks considering the ongoing dose, drug half-life and appearance of discontinuation syndrome.
- The approved medications in children include sertraline (6 years and older), fluoxetine (8 years and older), fluvoxamine (8 years and older), citalopram (12-18 years), escitalopram (12-18 years) and clomipramine (10 years and older).

### Pregnancy

- Anxiety symptoms and disorders are common during pregnancy and prevalence can be as high as 15% in pregnant women.
- Psychological intervention (CBT) is the preferred choice in pregnant women with anxiety disorders.
- SSRI is the first choice when symptoms are severe or disabling.
- Decision to initiate drug therapy should be considered on individual case basis.
- For newly diagnosed anxiety disorders during pregnancy, if possible, avoid drug therapy during first trimester.
- Benefit vs. risk of continuing SSRIs during pregnancy should be assessed and discussed taking into consideration that discontinuation may lead to relapse.
- Lorazepam, diazepam and clonazepam can be used for short-term control of anxiety symptoms. Promethazine can be used as a hypnotic.
- Increased support should be offered in the postnatal period.
- Pharmacotherapy should be maintained for at least six months after therapeutic response.

### Lactating mothers

- Mothers should be encouraged to continue breastfeeding their infants.
- Sertraline or fluoxetine is preferred for lactating mothers.
- Benzodiazepine with short half-life like lorazepam can be considered for acute management of anxiety symptoms.
- Pharmacotherapy should be maintained for at least six months after therapeutic response.

### Elderly

- SSRIs are effective in treating anxiety disorders in older population and better tolerated than other medications.
- SSRIs can cause hyponatremia and syndrome of inappropriate diuretic hormone secretion (SIADH) in elderly. Also, they increase risk of gastrointestinal bleeding. Consider risk factors for bleeding like previous bleeding history, concomitant use of NSAIDs, steroids and anticoagulants before prescribing SSRIs.
- Duloxetine, venlafaxine, pregabalin and quetiapine have also shown efficacy in older population.
- CBT is also effective for older adults with anxiety disorders.

**Table 13: Recommended therapy in special population**

| | |
|---|---|
| Children and adolescents | CBT<br>SSRIs (Sertraline, Fluoxetine, Fluvoxamine)<br>Clomipramine |
| Pregnant women | CBT<br>SSRIs<br>Lorazepam, Diazepam, Clonazepam<br>(Short-term use)<br>Promethazine |
| Lactating mothers | CBT<br>SSRIs (Sertraline, Fluoxetine)<br>Lorazepam |
| Elderly | CBT<br>SSRIs<br>SNRIs (Duloxetine, Venlafaxine)<br>Pregabalin<br>Quetiapine |

# CHAPTER 5
# OTHER ISSUES

## 5.1 Prognosis of anxiety disorders

### Specific phobia

Specific phobia usually begins in childhood and when persist into adulthood continue to persist for many years. The severity of the phobia remains relatively constant, without waxing and waning course seen in other anxiety disorders.

### Social anxiety disorder

It tends to become a chronic disorder. Many individuals with SAD are not aware of their mental health problems and, therefore, do not seek treatment. SAD is associated with suicidal tendency, low self-esteem, lower socioeconomic status, unemployment, financial issues, etc.

### Panic disorder

It is chronic disorder with variable course both among patients and within a single patient. At long-tern follow up, 30-40% of patients appear symptom free, about 50% have mild symptoms and about 10-20% continue to experience significant symptoms. Depression, substance use, suicidal tendency may develop during the course of illness.

### Agoraphobia

The course of agoraphobia is persistent and chronic, with complete remission being relatively rare except with treatment or intervention. Most cases of agoraphobia are thought to be caused by panic disorder. With treatment, most patients exhibit dramatic improvement in the symptoms of panic disorder and agoraphobia.

### Generalized anxiety disorder

If untreated, GAD usually takes a chronic course, with most patients still suffering from its symptoms six to twelve years after the diagnosis is made. Relapses are common and overall, the quality of life of these patients is poor.

## 5.2 Management in primary health care

**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

**Assess (check the box for common symptoms)**
Onset of anxiety symptoms
Nature of symptoms (worry, avoidance, obsession)
Any life event or trauma
Impact on current functioning

**Exclude medical conditions that can present with anxiety symptoms like**
Hyperthyroidism, Cardiopulmonary disorders, Traumatic brain injury, Hypoglycemia, Epilepsy, Substance use

**Mild or greater problem burden**

**Identify specific anxiety disorder**
**(For detail diagnostic criteria see glossary)**

Specific phobia

- Is your fear or anxiety associated with avoiding or doing an activity or being in contact with an object or animal or being in a particular environment (flights, heights)?
- Do you think your fear is excessive or unreasonable in some way?

SAD

- 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?

Panic disorder

- 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?

Agoraphobia

- Fear of places or situations where getting help or escape might be difficult, such as in a crowd or on a bridge?
- Are you afraid of going out of the house, being in crowds or taking public transport?
- Do you need to be accompanied by someone to be able to undertake these activities?

GAD

- 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?

## Manage anxiety disorders

**Non-pharmacological**

- Psychoeducation to the person and their carers about treatment options and medications
- Reduce stress and strengthen social supports
- Promote functioning in daily activities and community life
- If available, consider referral to a psychiatrist for evaluation and cognitive behavioral therapy (CBT).

**Pharmacological**

- Antidepressant: adequate dose and duration (see management chapter for special populations)
- DO NOT manage the symptoms with ineffective treatments
- Offer regular follow-up

**Antidepressants**

**SSRI:** Fluoxetine: Start 20 mg daily. If no response in 6 weeks, increase to 40 mg.
Sertraline: Start 25 mg at morning/daytime. Increase by 25-50 mg per week to 100-150 mg.

Add short-term (maximum 3 weeks) Benzodiazepine for severe symptoms (e.g., Diazepam 5 mg, Clonazepam 0.5 mg, Alprazolam 0.25 mg once or twice daily.

- SSRI works slowly, so patients and doctors both need patience.
- Need to continue for six months or longer after resolution of symptoms.
- If no improvement after 6-8 weeks, refer the patient to a psychiatrist.

**FGD findings**

Bangladesh Association of Psychiatrists (BAP) organized several focus group discussions (FGD) with senior psychiatrists, general physicians and persons with living experience of anxiety disorders to understand the current treatment approach and pattern in managing patients with anxiety disorders in Bangladesh. They each had more than 25 years of psychiatric clinical experience, practiced in variety of settings ranging from very low resource settings, government hospitals to top notch corporate hospitals. We asked them about their usual treatment choices in different anxiety disorders - the following table summarizes their most common responses.

Drug non-compliance is a point of concern and to ensure compliance strategies like psycho education, involvement of family members, starting drugs at lower dosage, choosing more tolerable drug, regular monitoring of side effects, regular follow up were suggested by them.

General physicians were of different sub divisions of medical science; they described that they are aware of sign-symptoms of anxiety disorders in most cases but cannot make specific diagnosis; in mild cases they try to manage the patient themselves and in more severe or unremitting cases refer to psychiatric department of medical college hospital consequently. To get a proper diagnosis, patients often had to visit several physicians and sometimes there were long duration between symptom onset and first consultation.

**Table 14: Commonly prescribed drugs in Bangladesh – findings from FGD with psychiatrists**

| | |
|---|---|
| Specific phobia | SSRI, Benzodiazepine (short acting), Imipramine, Propranolol, CBT if available |
| Social anxiety disorder | SSRI, Benzodiazepine (short acting), Propranolol, CBT if available |
| Panic disorder | SSRI, Benzodiazepine |
| Agoraphobia | SSRI, Benzodiazepine, Imipramine, Propranolol |
| Generalized anxiety disorder | SSRI, Benzodiazepine, Propranolol, Imipramine |

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# ANNEXURES

**Table 15: Anxiety disorders: short description according to DSM-5 classification**

| | |
|---|---|
| Specific phobia | Phobias which are restricted to singular, circumscribed situations, often related to animals (e.g., cats, spiders, or insects), natural phenomena (e.g., blood, heights, deep water), blood-injection-injury (e.g., needles, medical procedures), situations (e.g., airplanes, elevators, closed spaces) and other situations like choking, vomiting, etc. |
| Social anxiety disorder (social phobia) | Patients are afraid of situations in which they are the center of attention and may be criticized—e.g., public speaking, class rooms, board meetings, visit to authorities, conversations with superiors on the job, or with persons of the opposite sex. They are afraid of appearing clumsy, embarrassing themselves, or being judged negatively. |
| Panic disorder | Anxiety attacks of sudden onset, with physical manifestations of anxiety (e.g., palpitations, sweating, tremor, dry mouth, dyspnea, feeling of choking; chest pain; abdominal discomfort; feeling of unreality, paresthesia, collapse, impending death, going mad, etc.). Panic attacks can arise out of the blue; moreover, many patients start to avoid situations in which they fear that panic attacks might occur. |
| Agoraphobia | Fear of places where it might be difficult or embarrassing to escape if a panic attack should occur (crowds, on public transport, in closed spaces, e.g., elevators, open spaces, away from home, standing in long cue). Fear of being alone is also common. |
| Generalized anxiety disorder | Anxiety, worry, tension and fears about everyday events and problems. Patients suffer from excessive worry along with somatic anxiety symptoms (tremor, palpitations, dizziness, nausea, muscle tension, etc.) and from psychological symptoms, including difficulty concentrating, nervousness, insomnia, irritability, restlessness, etc. |

## Table 16: List of drugs used in anxiety disorders

| Class | Drug |
|---|---|
| SSRIs | Citalopram, Escitalopram, Fluoxetine, Fluvoxamine, Paroxetine, Sertraline |
| SNRIs | Duloxetine, Venlafaxine |
| TCAs | Amitriptyline, Clomipramine, Imipramine |
| NaSSA | Mirtazapine |
| Calcium modulator | Pregabalin |
| Azapirone | Buspirone |
| Melatonin agonist | Agomelatine |
| MAOIs | *Phenelzine, Moclobemide* |
| Antipsychotic | Olanzapine, Quetiapine, Risperidone, Ziprasidone |
| Mood stabilizers | Levetiracetam, Lithium, Topiramate, Valproate |
| Benzodiazepine | Alprazolam, Bromazepam, Chlordiazepoxide Clonazepam, Diazepam, Lorazepam, Oxazepam |
| Beta blocker | Propranolol, Pindolol |
| Antihistamine | Hydroxyzine |

*Drugs are listed alphabetically, Italics are not available in Bangladesh market*

**Table 17: Recommended psychological treatment for specific phobia**

| Therapy | Indication |
|---|---|
| Exposure-based treatments | All specific phobias |
| Virtual reality exposure | Heights, flying, spiders, claustrophobia and fears for which in vivo exposure may not be practical (e.g., fear of storms) |
| Computer-based self-help programs | Spiders, flying, small animals |
| Applied muscle tension (exposure combined with muscle tension exercises) Stress-reducing medical devices, such as decorated butterfly needles and syringes | Blood-injection-injury type |
| Cognitive behavior therapy and exposure | Dental, flying |

**Table 18: Adverse effects of drugs used in anxiety disorders**

| | |
|---|---|
| **SSRIs** | |
| GIT | Nausea, appetite change, dry mouth, diarrhea, constipation, dyspepsia, vomiting, weight loss |
| Central nervous system | Headache, insomnia, dizziness, anxiety, fatigue, tremor, impaired concentration, somnolence, extrapyramidal side effects, seizures, mania, akathisia, restlessness |
| Others | Suicidal ideation, delayed orgasm, anorgasmia, rash, pharyngitis, dyspnea, serum sickness, hyponatremia, alopecia, arthralgia, serotonin syndrome, severe cutaneous adverse reactions (SCARs), syndrome of inappropriate ADH secretion (SIADH), thrombocytopenia, discontinuation syndrome |
| **TCAs** | |
| GIT | Dry mouth, constipation, weight gain |
| Central nervous system | Drowsiness, sedation, seizures, cognitive impairment |
| Cardiovascular | Tachycardia, postural hypotension, cardiac conduction defects, arrhythmias, oedema |
| Others | Blurred vision, glaucoma, urinary retention, sexual dysfunction, rash, leucopenia, elevated liver enzymes |
| **Benzodiazepines** | |
| | Alertness decreased, ataxia (more common in elderly) confusion (more common in elderly), dizziness, drowsiness, dysarthria, fatigue, gastrointestinal disorder, headache, hypotension, muscle weakness, nausea, sleepiness, tremor, vertigo, vision problem, withdrawal syndrome, dependence. |
| **SNRIs** | |
| | Anxiety, appetite decreased, altered taste, arrhythmias, asthenia, chills, constipation, diarrhea, dizziness, dry mouth, headache, hot flush, hypertension, menstrual cycle irregularities, vision problem, nausea, vomiting, sleep problem, sweat change, weight changes, yawning |

**Table 19: Managing common side effects**

| Side effects | Management strategies |
|---|---|
| GIT symptoms | Can be minimized by starting with low doses and taking in full stomach<br>If mild queasiness or nausea occurs, it will usually disappear within 1–2 weeks at a constant dose<br>Proton pump inhibitors |
| GIT bleeding | Use with caution when aspirin, NSAIDs or anticoagulants is co-prescribed |
| Insomnia | Taking medication in the morning<br>Following standard sleep hygiene practice<br>Benzodiazepines or zolpidem |
| Fatigue or sleepiness | Can be minimized by starting with low doses<br>Night dosing<br>Addition of modest doses of Modafinil |
| Agitation | Increase the dose gradually<br>Benzodiazepine |
| Sweating | Low doses of anticholinergic agents such as Benztropine or with Clonidine, Cyproheptadine and Mirtazapine |
| Sexual side-effects | Can be minimized by starting with low doses or reducing the dose to the minimal effective dose<br>Drug holiday: trying a once-weekly, one-day drug holiday before engaging in sexual activity<br>Switching to another SSRI<br>Adding a counteracting pharmacologic agent<br>For restoring libido: Amantadine, Buspirone, Yohimbine, Ginkgo Biloba extract, Cyproheptadine<br>For restoring erection and orgasmic ability: Sildenafil, Tadalafil, Vardenafil. |
| Hyponatremia | Common in elderly<br>Monitor patients<br>Refer if serum sodium level < 125 mmol/L |
| Weight gain | Dietary modification and exercise<br>Topiramate may be tried<br>If significant, switch to another SSRI |
| Suicidal behavior | Children and adolescent may show increase in suicidal thoughts<br>Monitor specially during the first 10 days |
| Discontinuation syndrome | Withdraw gradually<br>Taper no more than 25% per week<br>Reintroduction of long-acting SSRI (Fluoxetine) |

# Glossary

## DSM-5 diagnostic criteria for different disorders

**Specific phobia**

A. Marked fear or anxiety about a specific object or situation (e.g., flying, heights, animals, receiving an injection, seeing blood). Note: In children, the fear or anxiety may be expressed by crying, tantrums, freezing, or clinging.

B. The phobic object or situation almost always provokes immediate fear or anxiety.

C. The phobic object or situation is actively avoided or endured with intense fear or anxiety.

D. The fear or anxiety is out of proportion to the actual danger posed by the specific object or situation and to the sociocultural context.

E. The fear, anxiety, or avoidance is persistent, typically lasting for 6 months or more.

F. The fear, anxiety, or avoidance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

G. The disturbance is not better explained by the symptoms of another mental disorder, including fear, anxiety, and avoidance of situations associated with panic-like symptoms or other incapacitating symptoms (as in agoraphobia): objects or situations related to obsessions (as in obsessive-compulsive disorder); reminders of traumatic events (as in posttraumatic stress disorder); separation from home or attachment figures (as in separation anxiety disorder); or social situations (as in social anxiety disorder).

**Social anxiety disorder (social phobia)**

A. Marked fear or anxiety about one or more social situations in which the individual is exposed to possible scrutiny by others. Examples include social interactions (e.g., having a conversation, meeting unfamiliar people), being observed (e.g., eating or drinking), and performing in front of others (e.g., giving a speech).

Note: In children, the anxiety must occur in peer settings and not just during interactions with adults.

B. The individual fears that he or she will act in a way or show anxiety symptoms that will be negatively evaluated (i.e., will be humiliating or embarrassing: will lead to rejection or offend others).

C. The social situations almost always provoke fear or anxiety.

Note: In children, the fear or anxiety may be expressed by crying, tantrums, freezing, clinging, shrinking, or failing to speak in social situations.

D. The social situations are avoided or endured with intense fear or anxiety.

E. The fear or anxiety is out of proportion to the actual threat posed by the social situation and to the sociocultural context.

F. The fear, anxiety, or avoidance is persistent, typically lasting for 6 months or more.

G. The fear, anxiety, or avoidance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

H. The fear, anxiety, or avoidance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition.

I. The fear, anxiety, or avoidance is not better explained by the symptoms of another mental disorder, such as panic disorder, body dysmorphic disorder, or autism spectrum disorder.

J. If another medical condition (e.g., Parkinson's disease, obesity, disfigurement from bums or injury) is present, the fear, anxiety, or avoidance is clearly unrelated or is excessive.

**Panic disorder**

A. Recurrent unexpected panic attacks. A panic attack is an abrupt surge of intense fear or intense discomfort that reaches a peak within minutes, and during which time four (or more) of the following symptoms occur;

Note: The abrupt surge can occur from a calm state or an anxious state.

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.

Note: Culture-specific symptoms (e.g., tinnitus, neck soreness, headache, uncontrollable screaming or crying) may be seen. Such symptoms should not count as one of the four required symptoms.

B. At least one of the attacks has been followed by 1 month (or more) of one or both of the following:

1. Persistent concern or worry about additional panic attacks or their consequences (e.g., losing control, having a heart attack, "going crazy").

2. A significant maladaptive change in behavior related to the attacks (e.g., behaviors designed to avoid having panic attacks, such as avoidance of exercise or unfamiliar situations).

C. The disturbance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition (e.g., hyperthyroidism, cardiopulmonary disorders).

D. The disturbance is not better explained by another mental disorder (e.g., the panic attacks do not occur only in response to feared social situations, as in social anxiety disorder: in response to circumscribed phobic objects or situations, as in specific phobia: in response to obsessions, as in obsessive-compulsive disorder: in response to reminders of traumatic events, as in posttraumatic stress disorder: or in response to separation from attachment figures, as in separation anxiety disorder).

**Agoraphobia**

A. Marked fear or anxiety about two (or more) of the following five situations:

1. Using public transportation (e.g., automobiles, buses, trains, ships, planes).

2. Being in open spaces (e.g., parking lots, marketplaces, bridges).

3. Being in enclosed places (e.g., shops, theaters, cinemas).

4. Standing in line or being in a crowd.

5. Being outside of the home alone.

B. The individual fears or avoids these situations because of thoughts that escape might be difficult or help might not be available in the event of developing panic-like symptom or other incapacitating or embarrassing symptoms (e.g., fear of falling in the elderly; fear of incontinence).

C. The agoraphobic situations almost always provoke fear or anxiety.

D. The agoraphobic situations are actively avoided, require the presence of a companion, or are endured with intense fear or anxiety.

E. The fear or anxiety is out of proportion to the actual danger posed by the agoraphobic situations and to the sociocultural context.

F. The fear, anxiety, or avoidance is persistent, typically lasting for 6 months or more.

G. The fear, anxiety, or avoidance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

H. If another medical condition (e.g., inflammatory bowel disease, Parkinson's disease) is present, the fear, anxiety, or avoidance is clearly excessive.

I. The fear, anxiety, or avoidance is not better explained by the symptoms of another mental disorder—for example, the symptoms are not confined to specific phobia, situational type; do not involve only social situations (as in social anxiety disorder): and are not related exclusively to obsessions (as in obsessive-compulsive disorder), perceived defects or flaws in physical appearance (as in body dysmorphic disorder), reminders of traumatic events (as in posttraumatic stress disorder), or fear of separation (as in separation anxiety disorder).

**Generalized Anxiety Disorder**

A. Excessive anxiety and worry (apprehensive expectation), occurring more days than not for at least 6 months, about a number of events or activities (such as work or school performance).

B. The individual finds it difficult to control the worry.

C. The anxiety and worry are associated with three (or more) of the following six symptoms (with at least some symptoms having been present for more days than not for the past 6 months);

Note: Only one item is required in children.

1. Restlessness or feeling keyed up or on edge.

2. Being easily fatigued.

3. Difficulty concentrating or mind going blank.

4. Irritability.

5. Muscle tension.

6. Sleep disturbance (difficulty falling or staying asleep, or restless, unsatisfying sleep).

D. The anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

E. The disturbance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition (e.g., hyperthyroidism).

F. The disturbance is not better explained by another mental disorder (e.g., anxiety or worry about having panic attacks in panic disorder, negative evaluation in social anxiety disorder [social phobia], contamination or other obsessions in obsessive-compulsive disorder, separation from attachment figures in separation anxiety disorder, reminders of traumatic events in posttraumatic stress disorder, gaining weight in anorexia nervosa, physical complaints in somatic symptom disorder, perceived appearance flaws in body dysmorphic disorder, having a serious illness in illness anxiety disorder, or the content of delusional beliefs in schizophrenia or delusional disorder).