CHAPTER 6

TREATMENT ALGORITHMS FOR PSYCHIATRIC DISORDERS

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Abstract

Psychiatric treatment algorithms are guideline-based, measurement-informed, and highly individualized, with a dual focus on symptom remission and functional recovery. The algorithm for Major Depressive Disorder (MDD) is a stepwise approach, beginning with first-line psychotherapy (e.g., CBT) or pharmacotherapy (e.g., SSRI/SNRI). Failure of an adequate trial (6-8 weeks) triggers a subsequent step, such as switching to a different agent or augmenting with a second medication (e.g., bupropion, aripiprazole). The algorithm for anxiety disorders (e.g., GAD) is similar, prioritizing CBT, SSRIs, or SNRIs, with agents like buspirone or pregabalin as second-line or adjunctive options; benzodiazepines are reserved for short-term, acute management. The algorithm for schizophrenia is stratified by treatment response. First-line therapy is a second-generation antipsychotic (SGA). Treatment resistance, defined by failure of two different antipsychotic trials, is a specific indication to advance the algorithm to clozapine. The algorithm for bipolar disorder is bifurcated by the patient's acute state. Mania is managed with mood stabilizers (e.g., lithium, valproate) or SGAs, whereas bipolar depression is treated with agents with specific efficacy for this phase (e.g., lurasidone, quetiapine), strictly avoiding antidepressant monotherapy.

Keywords: *Psychiatric Algorithms, Major Depressive Disorder, Anxiety Disorders, Schizophrenia, Bipolar Disorder, Pharmacotherapy*

Learning Objectives

After completion of the chapter, the learners should be able to:

- List first-line pharmacological classes (e.g., SSRIs, SNRIs) for Major Depressive Disorder and Generalized Anxiety Disorder.
- Explain the algorithm for managing an acute manic episode in a patient with Bipolar I Disorder, emphasizing the need for mood stabilization.
- Formulate a treatment augmentation plan for a patient with treatment-resistant depression.
- Differentiate the treatment algorithm for a positive-symptom-predominant schizophrenic episode versus a negative-symptom-predominant presentation.
- Justify the selection of a second-generation (atypical) antipsychotic over a first-generation (typical) agent for a newly diagnosed patient.

MAJOR DEPRESSIVE DISORDER

Major Depressive Disorder is a common and serious mood disorder characterized by a persistent low mood and/or anhedonia, causing significant impairment. The treatment algorithm is a stepwise, measurement-based approach aimed at achieving full remission.

Pathophysiology

The pathophysiology of Major Depressive Disorder (MDD) is complex and not fully elucidated, extending well beyond the traditional "monoamine hypothesis." While a deficiency in monoamine neurotransmitters (serotonin, norepinephrine, and dopamine) provides a framework for understanding antidepressant action, it is an incomplete explanation. Modern theories incorporate a neuro-circuitry and neurotrophic perspective. Chronic stress is known to dysregulate the hypothalamic-pituitary-adrenal (HPA) axis, leading to sustained high levels of cortisol. This hypercortisolemia is toxic to the hippocampus, a key brain region for mood regulation and memory. This leads to the "neurotrophic hypothesis," which posits that depression is associated with reduced brain-derived neurotrophic factor (BDNF), leading to atrophy and reduced

neurogenesis in the hippocampus and prefrontal cortex. Antidepressants, in this model, may work by increasing BDNF, promoting synaptic plasticity, and restoring these crucial neural circuits.

Diagnosis

Diagnosis is made by fulfilling the DSM-5 criteria: at least five of nine symptoms (including depressed mood or anhedonia) for at least two weeks (often recalled by the mnemonic SIGECAPS: Sleep, Interest, Guilt, Energy, Concentration, Appetite, Psychomotor, Suicidality). The severity is assessed (mild, moderate, severe) to guide the initial algorithm.

Differential Diagnosis

The most critical differential is Bipolar-Disorder; diagnosing MDD and prescribing an antidepressant in a patient with bipolar disorder can induce mania or rapid cycling. This is the "MDD vs. Bipolar" pitfall. Medical differentials must be excluded, including hypothyroidism, anemia, vitamin deficiencies (B12, D), and neurological conditions (e.g., Parkinson's, stroke). Substance-induced depression (e.g., from alcohol, beta-blockers) and other psychiatric disorders (e.g., anxiety, adjustment disorder) must also be considered.

Treatment Algorithm

The algorithm is stratified by severity but generally follows a stepwise progression after an inadequate response to the prior step. An adequate trial is defined as 6-8 weeks at a therapeutic dose.

- **Step 1: First-Line Therapy:**
    - **Mild-Moderate MDD:** Psychotherapy (e.g., Cognitive Behavioral Therapy [CBT], Interpersonal Therapy [IPT]) OR a first-line antidepressant is appropriate.
    - **Moderate-Severe MDD:** Pharmacotherapy is the cornerstone, often in combination with psychotherapy. First-line agents include Selective Serotonin Reuptake Inhibitors

(SSRIs) or Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs). Bupropion or mirtazapine may also be first-line, chosen based on symptom profile (e.g., bupropion for low energy, mirtazapine for insomnia/anorexia).

- **Step 2: First Treatment Failure:** If an adequate trial of an SSRI fails:
    - **Switch:** Change to a different agent within the same class (another SSRI) or to a different class (e.g., an SNRI, bupropion).
    - **Augment:** Add a second agent. Common evidence-based augmentation algorithms include adding bupropion to an SSRI, or adding an atypical (second-generation) antipsychotic (e.g., aripiprazole, quetiapine XR, olanzapine).
- **Step 3: Second Treatment Failure:** If a second trial (either switch or augmentation) fails, the algorithm proceeds to:
    - **Switch:** Change to a less common class, such as a tricyclic antidepressant (TCA), requires more monitoring.
    - **Augment:** Add lithium or thyroid hormone (T3, liothyronine).
- **Step 4: Treatment-Resistant Depression (TRD):** Failure of ≥ 2-3 adequate trials defines TRD. This triggers consideration of neurostimulation techniques, including Electroconvulsive Therapy (ECT), which is the most effective algorithm for severe or catatonic depression. Transcranial Magnetic Stimulation (TMS) or intranasal esketamine are other options.

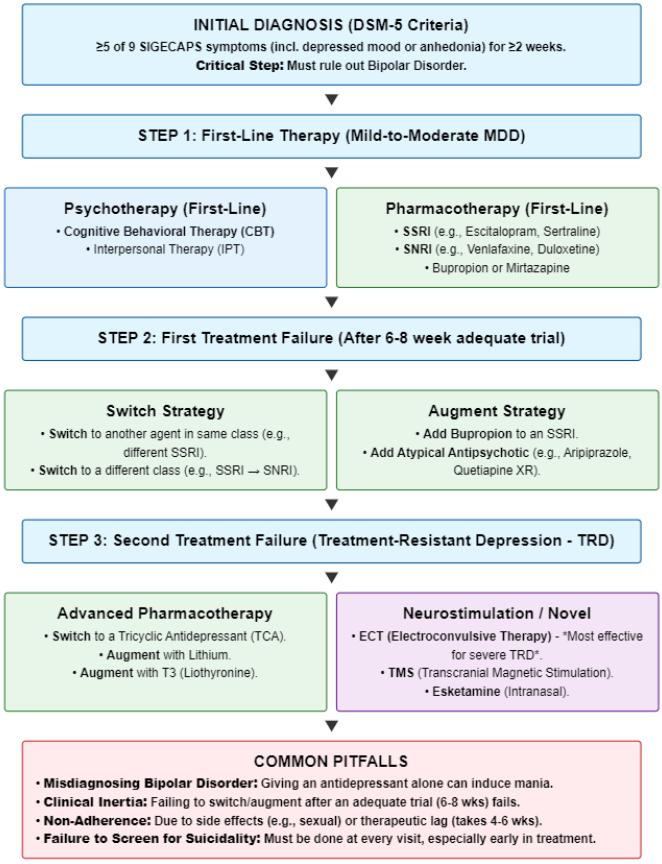

Figure 6.1: Major Depressive Disorder (MDD)

Monitoring and Follow-Up

Monitoring in MDD is primarily clinical and symptom-based. The first follow-up visit should occur within 2-4 weeks of initiating pharmacotherapy to assess for tolerability, side effects, and, critically, suicide risk. A "response" (a 50% reduction in symptoms) may not be evident for 4-6 weeks, while "remission" (the goal of treatment, where symptoms are absent) may take 8-12 weeks. Validated rating scales, such as the Patient Health Questionnaire-9 (PHQ-9), should be used at baseline and at

regular intervals (e.g., every 4-8 weeks) to objectively track symptom burden. Monitoring must also include a specific assessment for the emergence of agitation, anxiety, or suicidal ideation, which can (rarely) be an early activating effect of SSRIs, particularly in younger patients. Once a patient achieves remission, follow-up can be extended to every 3-6 months

Table 6.1: Stepwise Algorithm for Major Depressive Disorder (MDD)

Step	Intervention	Rationale / Goal
Step 1	First-Line Agent (e.g., SSRI, SNRI, Bupropion)	Initiate monotherapy. (SSRI e.g., Escitalopram is common first choice).
Step 2 (Inadequate Response)	**Switch** to a different first-line agent OR **Augment** with a second agent (e.g., Bupropion, Mirtazapine, or Atypical Antipsychotic).	Optimize response.
Step 3 (Inadequate Response)	Switch or Augment again. (Consider different classes).	Achieve remission.
Step 4 (Treatment-Resistant)	Refer for specialist consult. Consider options like ECT, TMS	Manage complex/refractory illness.

Long-Term Management / Secondary Prevention

The management of MDD is divided into three phases. The *Acute Phase* (6-12 weeks) aims to achieve remission. The *Continuation Phase* lasts for 4-9 *months after* remission is achieved; continuing the antidepressant at the full therapeutic dose during this time is the single most important factor in preventing a short-term relapse. For patients with a high risk of recurrence (e.g., three or more lifetime episodes, early age of onset, severe

episodes), *Maintenance Phase* therapy (lifelong antidepressant treatment) is the standard of care to prevent future episodes. Psychotherapy, particularly Cognitive Behavioral Therapy (CBT) or Interpersonal Therapy (IPT), is a first-line treatment and is highly effective for secondary prevention. The combination of pharmacotherapy and psychotherapy ("pills and skills") is considered the most effective long-term strategy.

Patient Counseling Points

1. **Therapeutic Lag:** This is the most important counseling point. The patient must understand that the antidepressant is not an "as-needed" pill and will take 4-6 weeks to exert its full effect, even though side effects may appear earlier.
2. **Adherence and Discontinuation:** Emphasize that the medication must be taken every day, even when they start to feel better, to prevent relapse. They must *never* stop the medication abruptly, as this can cause a "discontinuation syndrome" (flu-like symptoms, "brain zaps," anxiety).
3. **Side Effects:** Discuss common, transient side effects (e.g., nausea, headache) which often resolve in 1-2 weeks. Also discuss long-term side effects like sexual dysfunction or weight gain and encourage the patient to report them.
4. **Suicide Risk (Black Box Warning):** Patients under 25 (and their families) must be warned of the small, but real, risk of increased suicidal ideation or agitation in the first few weeks of treatment and told to report this immediately.
5. **Role of Psychotherapy:** Frame psychotherapy (CBT) as an active part of treatment that provides long-term skills to manage negative thought patterns and prevent future episodes.

Common Pitfalls in Management

The most critical pitfall is misdiagnosing Bipolar Disorder as unipolar MDD. Another is clinical inertia, failing to advance the algorithm after an inadequate trial, often due to insufficient dose

or duration. A major safety pitfall is the failure to repeatedly and directly screen for suicidal ideation. Finally, overlooking medical or substance-induced causes can lead to treating the wrong condition.

Case Study

A 32-year-old female (Ms. Allen) presents with a 2-month history of a persistent sad mood, loss of interest in her hobbies (anhedonia), low energy, difficulty concentrating, and feelings of worthlessness. Her PHQ-9 score is 18 (moderately severe). She has no personal or family history of mania or hypomania.

Discussion

This is a classic presentation of a first episode of **Major Depressive Disorder**. Given the moderately-severe symptoms impacting her function, the algorithm supports initiating first-line therapy (pharmacotherapy, psychotherapy, or both). The critical first step is to rule out Bipolar Disorder.

Treatment Algorithm

1. **Diagnosis:** Moderately-severe Major Depressive Disorder.
2. **Critical Pitfall Check:** You screen for any history of mania (e.g., "Have you ever had a period of days where you had so much energy you didn't need to sleep?"). She denies any, making an SSRI safe to prescribe.
3. **Algorithm Step 1 (First-Line):** You offer both psychotherapy (CBT) and pharmacotherapy. She agrees to both.
    - **Pharmacotherapy:** Start a first-line SSRI, **Sertraline 50 mg daily**.
4. **Counseling:** You counsel her on the "therapeutic lag" (it may take 4-6 weeks to feel the full effect) and common, transient side effects (e.g., nausea).
5. **Follow-up:** You schedule a follow-up in 2-4 weeks to assess for side effects and monitor for any (rare) increase in suicidal ideation, and another at 8 weeks to assess for a full response.

Outcome

Ms. Allen is started on Sertraline 50 mg daily and given a referral for Cognitive Behavioral Therapy (CBT).

ANXIETY DISORDERS

This category includes Generalized Anxiety Disorder (GAD), Panic Disorder (PD), and Social Anxiety Disorder (SAD). The treatment algorithms share a common foundation.

Pathophysiology

Anxiety disorders are believed to arise from dysregulation in the brain's "fear circuit." The amygdala, a central processing hub for fear and threat, becomes hyper-responsive, sending false alarms to the rest of the brain. This activity is normally modulated and "turned off" by the prefrontal cortex, but in anxiety, this top-down control is deficient. Neurochemically, this maps onto a dysregulation of several systems. The inhibitory neurotransmitter GABA is a key player; benzodiazepines work by enhancing GABA's "braking" effect on this circuit. Furthermore, the serotonin and norepinephrine systems, which originate in the brainstem and project widely, are believed to be dysregulated, which is why SSRIs and SNRIs (the first-line agents) are effective in "re-tuning" this circuit over time.

Diagnosis

Diagnosis is based on DSM-5 criteria, characterized by excessive, persistent, and debilitating worry (GAD), discrete, recurrent, and unexpected panic attacks (PD), or marked fear of social situations (SAD).

Differential Diagnosis

Medical conditions that mimic anxiety ("anxiety mimics") must be ruled out. The main differentials include hyperthyroidism, cardiac arrhythmias (e.g., SVT), pheochromocytoma, pulmonary embolism, and vestibular

dysfunction. Substance/medication-induced anxiety (e.g., caffeine, albuterol, stimulants, withdrawal syndromes) is also extremely common.

Treatment Algorithm

The algorithm for GAD is a representative model.

- **Step 1: First-Line Therapy:** Psychotherapy (CBT) is highly effective and considered first-line, equivalent to pharmacotherapy. First-line medications are SSRIs or SNRIs (e.g., venlafaxine XR, duloxetine). These agents may initially worsen anxiety, requiring a "start low, go slow" titration algorithm.
- **Step 2: Second-Line Therapy:** If an adequate SSRI/SNRI trial fails, the algorithm suggests:
    - **Switch:** Change to a different first-line agent (another SSRI or SNRI).
    - **Switch:** Change to a second-line agent, such as buspirone (GAD-specific, often better as augmentation) or pregabalin.
- **Step 3: Augmentation/Refractory:** For partial response, augmentation with buspirone or pregabalin is a common algorithm. Hydroxyzine can be used as a short-term, "as-needed" anxiolytic.
- **Algorithm for Acute/Panic Symptoms:** For acute panic attacks or severe, short-term anxiety, benzodiazepines (e.g., lorazepam, alprazolam) are highly effective. However, their algorithm is for short-term (< 2-4 weeks) or "as-needed" use only, to bridge the patient until long-term therapies (like SSRIs) take effect.

Monitoring and Follow-Up

Monitoring is clinical, tracking the frequency and severity of anxiety, panic attacks, and avoidance behaviors. The GAD-7 (for Generalized Anxiety Disorder) or Panic Disorder Severity Scale (PDSS) are useful objective tools. Follow-up should be scheduled 2-4 weeks after initiating an SSRI/SNRI to monitor for side effects, particularly the "jitteriness" or "activation syndrome," a common early side effect where anxiety transiently worsens. This is managed by "starting low and going