

TREATING SCHIZOPHRENIA

A Quick Reference Guide



Based on *Practice Guideline for the Treatment of Patients With Schizophrenia*, Second Edition, originally published in February 2004. A guideline watch, summarizing significant developments in the scientific literature since publication of this guideline, may be available in the Psychiatric Practice section of the APA web site at www.psych.org.

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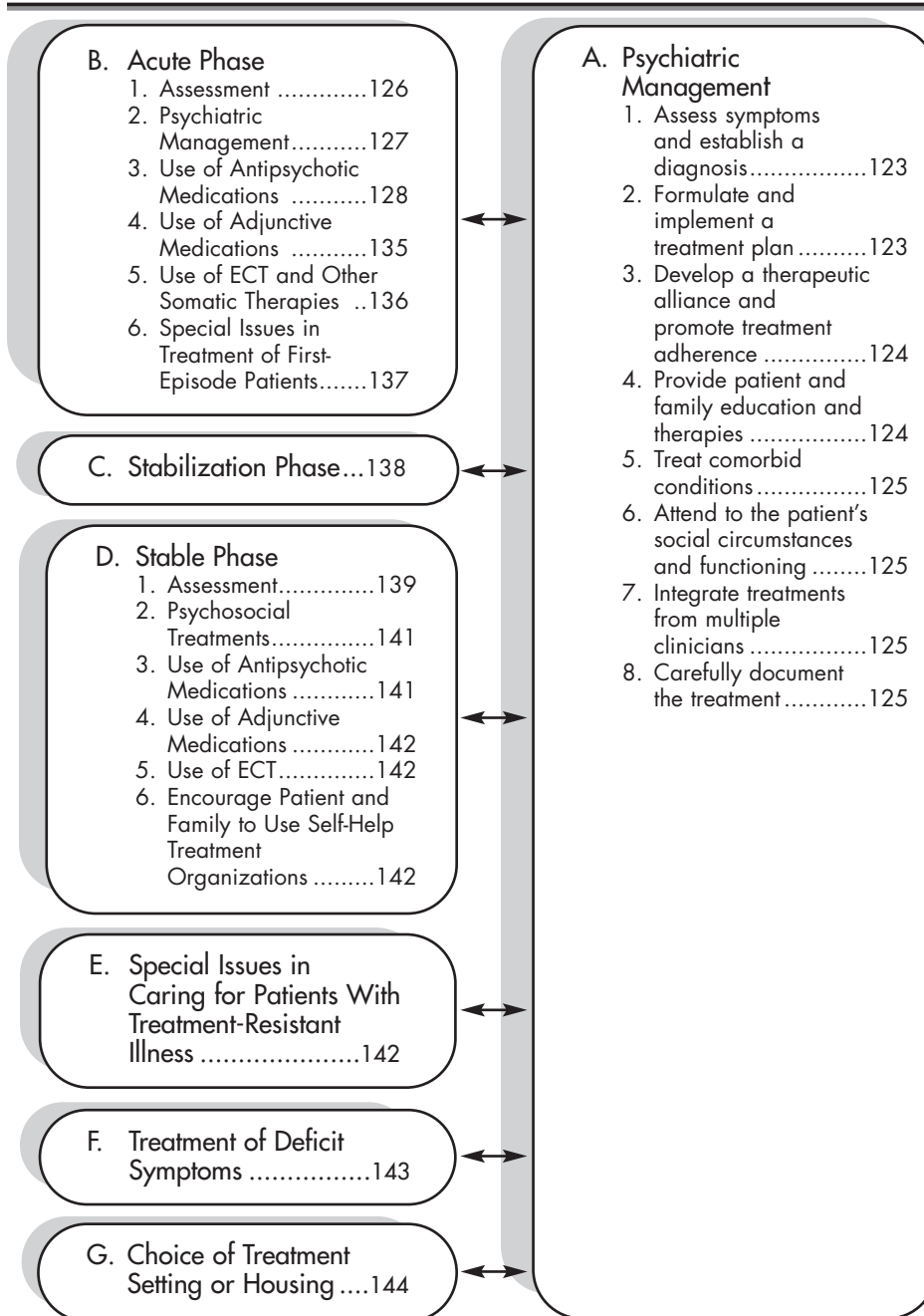
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Statement of Intent

The Practice Guidelines and the Quick Reference Guides are not intended to be construed or to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual patient and are subject to change as scientific knowledge and technology advance and practice patterns evolve. These parameters of practice should be considered guidelines only. Adherence to them will not ensure a successful outcome for every individual, nor should they be interpreted as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgment regarding a particular clinical procedure or treatment plan must be made by the psychiatrist in light of the clinical data presented by the patient and the diagnostic and treatment options available.

The development of the APA Practice Guidelines and Quick Reference Guides has not been financially supported by any commercial organization. For more detail, see APA's "Practice Guideline Development Process," available as an appendix to the compendium of APA practice guidelines, published by APPI, and online at http://www.psych.org/psych_pract/treatg/pg/prac_guide.cfm.

OUTLINE



A. Psychiatric Management

1. Assess symptoms and establish a diagnosis.

- Establish an accurate diagnosis, considering other psychotic disorders in the differential diagnosis because of the major implications for short- and long-term treatment planning. If a definitive diagnosis cannot be made but the patient appears prodromally symptomatic and at risk for psychosis, reevaluate the patient frequently.
- Reevaluate the patient's diagnosis and update the treatment plan as new information about the patient and his or her symptoms becomes available.
- Identify the targets of each treatment, use outcome measures that gauge the effect of treatment, and have realistic expectations about the degrees of improvement that constitute successful treatment.
- Consider the use of objective, quantitative rating scales to monitor clinical status (e.g., Abnormal Involuntary Movement Scale [AIMS], Structured Clinical Interview for DSM-IV Axis I Disorders [SCID], Brief Psychiatric Rating Scale [BPRS], Positive and Negative Syndrome Scale [PANSS]).

2. Formulate and implement a treatment plan.

- Select specific type(s) of treatment and the treatment setting. (This process is iterative and should evolve over the course of the patient's association with the clinician.)

3. Develop a therapeutic alliance and promote treatment adherence.

- Identify the patient's goals and aspirations and relate these to treatment outcomes to increase treatment adherence.
- Assess factors contributing to incomplete treatment adherence and implement clinical interventions (e.g., motivational interviewing) to address them. Factors contributing to incomplete treatment adherence include
 - patient's lack of insight about presence of illness or need to take medication,
 - patient's perceptions about lack of treatment benefits (e.g., inadequate symptom relief) and risks (e.g., unpleasant side effects, discrimination associated with being in treatment),
 - cognitive impairment,
 - breakdown of the therapeutic alliance,
 - practical barriers such as financial concerns or lack of transportation,
 - cultural beliefs, and
 - lack of family or other social support.
- Consider assertive outreach (including telephone calls and home visits) for patients who consistently do not appear for appointments or are nonadherent in other ways.

4. Provide patient and family education and therapies.

- Work with patients to recognize early symptoms of relapse in order to prevent full-blown illness exacerbations.
- Educate the family about the nature of the illness and coping strategies to diminish relapses and improve quality of life for patients.

5. Treat comorbid conditions, especially major depression, substance use disorders, and posttraumatic stress disorder.

6. Attend to the patient's social circumstances and functioning.

→ Work with team members, the patient, and the family to ensure that services are coordinated and that referrals for additional services are made when appropriate.

7. Integrate treatments from multiple clinicians.

8. Carefully document the treatment, since patients may have different practitioners over their course of illness.

B. Acute Phase

Goals of treatment

- Prevent harm.
- Control disturbed behavior.
- Reduce the severity of psychosis and associated symptoms (e.g., agitation, aggression, negative symptoms, affective symptoms).
- Determine and address the factors that led to the occurrence of the acute episode.
- Effect a rapid return to the best level of functioning.
- Develop an alliance with the patient and family.
- Formulate short- and long-term treatment plans.
- Connect the patient with appropriate aftercare in the community.

1. Assessment in the Acute Phase

Goals of acute phase assessment

- Evaluate the reason for the recurrence or exacerbation of symptoms (e.g., medication nonadherence).
- Determine or verify the patient's diagnosis.
- Identify any comorbid psychiatric or medical conditions, including substance use disorders.
- Evaluate general medical health.
- Identify the patient's strengths and limitations.
- Engage the patient in a therapeutic alliance.

Undertake a thorough initial workup, including complete psychiatric and general medical histories and physical and mental status examinations.

Routinely interview family members or other individuals knowledgeable about the patient, unless the patient refuses to grant permission.

In emergency circumstances (e.g., safety risk), it may be necessary and permissible to speak with others without the patient's consent.

Conduct laboratory tests, including a complete blood count (CBC); measurements of blood electrolytes and glucose; tests of liver, renal, and thyroid function; a syphilis test; and, when indicated, a urine or serum toxicology screen, hepatitis C test, and determination of HIV status.

- Consider use of a computed tomography (CT) or magnetic resonance imaging (MRI) scan (MRI is preferred) for patients with a new onset of psychosis or with an atypical clinical presentation, because findings (e.g., ventricular enlargement, diminished cortical volume) may enhance confidence in the diagnosis and provide information relevant to treatment planning and prognosis.
- Assess risk factors for suicide (such as prior attempts, depressed mood, suicidal ideation, presence of command hallucinations, hopelessness, anxiety, extrapyramidal side effects, and alcohol or other substance use).
- Assess likelihood of dangerous or aggressive behavior, including potential for harm to others.

2. Psychiatric Management in the Acute Phase

- Reduce overstimulating or stressful relationships, environments, and life events.
- Provide the patient with information (appropriate to his or her ability to assimilate) on the nature and management of the illness.
- Initiate a relationship with family members. Refer family members to local chapters of the National Alliance for the Mentally Ill (NAMI) and to the NAMI web site (www.nami.org).

3. Use of Antipsychotic Medications in the Acute Phase

- Initiate antipsychotic medication as soon as it is feasible. It may be appropriate to delay pharmacologic treatment for patients who require more extensive diagnostic evaluation or who refuse medications or if psychosis is caused by substance use or acute stress reactions.
- Discuss risks and benefits of the medication with the patient before initiating treatment, if feasible, and identify target symptoms (e.g., anxiety, poor sleep, hallucinations, and delusions) and acute side effects (e.g., orthostatic hypotension, dizziness, dystonic reactions, insomnia, and sedation).
- Assess baseline levels of signs, symptoms, and laboratory values relevant to monitoring effects of antipsychotic therapy.
 - Measure vital signs (pulse, blood pressure, temperature).
 - Measure weight, height, and body mass index (BMI), which can be calculated with the formula $\text{weight in kilograms}/(\text{height in meters})^2$ or the formula $703 \times \text{weight in pounds}/(\text{height in inches})^2$ or with a BMI table:
www.niddk.nih.gov/health/nutrit/pubs/statobes.htm#table
 - Assess for extrapyramidal signs and abnormal involuntary movements.
 - Screen for diabetes risk factors and measure fasting blood glucose.
 - Screen for symptoms of hyperprolactinemia.
 - Obtain lipid panel.
 - Obtain ECG and serum potassium measurement before treatment with thioridazine, mesoridazine, or pimozide; obtain ECG before treatment with ziprasidone in the presence of cardiac risk factors.
 - Conduct ocular examination, including slit-lamp examination, when beginning antipsychotics associated with increased risk of cataracts.
 - Screen for changes in vision.
 - Consider a pregnancy test for women with childbearing potential.

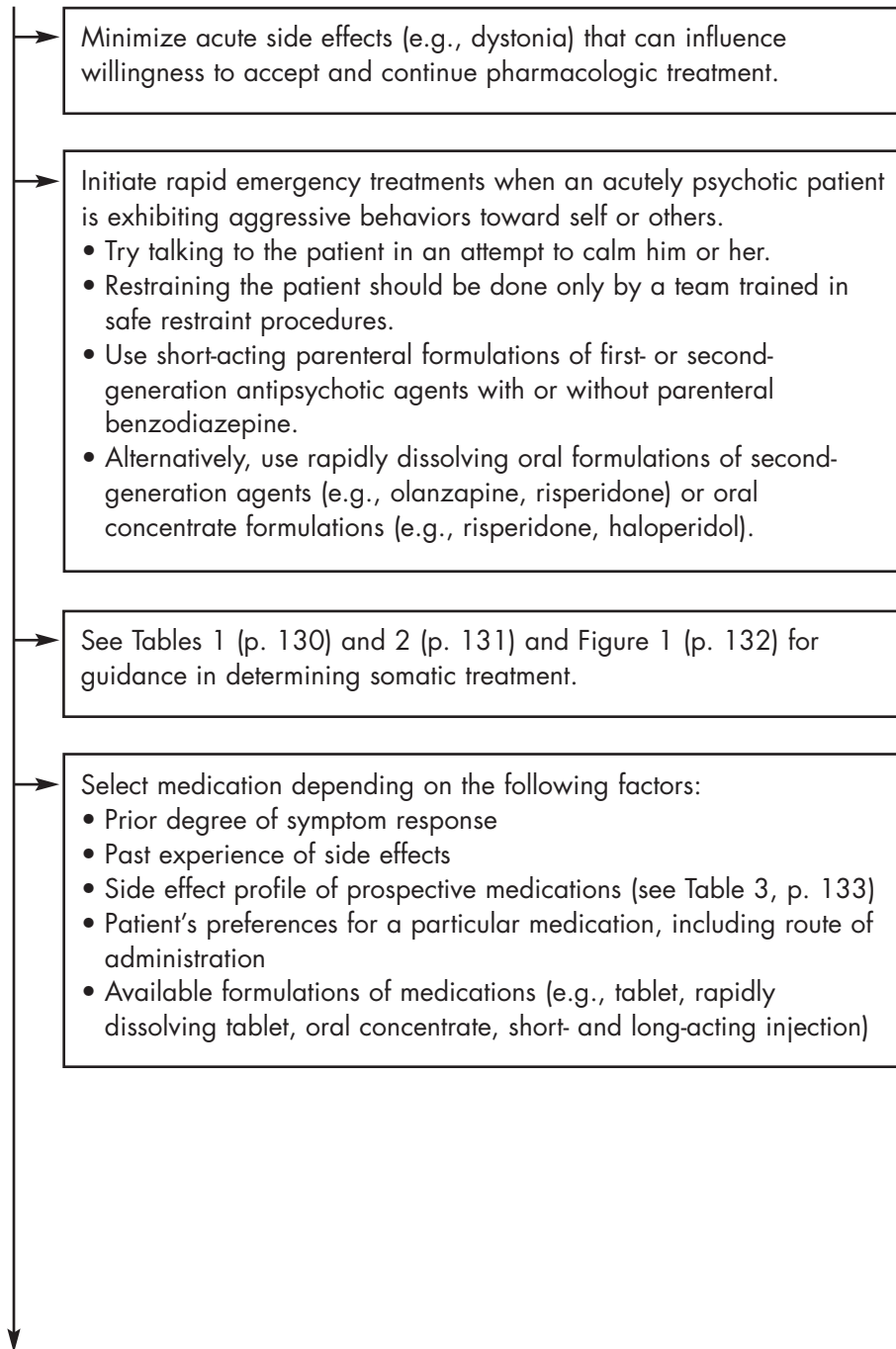


TABLE 1. Commonly Used Antipsychotic Medications

Antipsychotic Medication	Recommended Dose Range (mg/day) ^a	Chlorpromazine Equivalents (mg/day) ^b	Half-Life (hours) ^c
First-generation agents			
<i>Phenothiazines</i>			
Chlorpromazine	300–1000	100	6
Fluphenazine	5–20	2	33
Mesoridazine	150–400	50	36
Perphenazine	16–64	10	10
Thioridazine	300–800	100	24
Trifluoperazine	15–50	5	24
<i>Butyrophenone</i>			
Haloperidol	5–20	2	21
<i>Others</i>			
Loxapine	30–100	10	4
Molindone	30–100	10	24
Thiothixene	15–50	5	34
Second-generation agents			
Aripiprazole	10–30		75
Clozapine	150–600		12
Olanzapine	10–30		33
Quetiapine	300–800		6
Risperidone	2–8		24
Ziprasidone	120–200		7

^aDose range recommendations are adapted from the 2003 Schizophrenia Patient Outcome Research Team recommendations (Lehman AF, Kreyenbuhl J, Buchanan RW, et al.: "The Schizophrenia Patient Outcomes Research Team (PORT): Updated Treatment Recommendations 2003." *Schizophr Bull* [in press]).

^bChlorpromazine equivalents represent the approximate dose equivalent to 100 mg of chlorpromazine (relative potency). Chlorpromazine equivalents are not relevant to the second-generation antipsychotics; therefore, no chlorpromazine equivalents are indicated for these agents (Centorrino F, Eakin M, Bahk WM, et al.: "Inpatient Antipsychotic Drug Use in 1998, 1993, and 1989." *Am J Psychiatry* 159:1932–1935, 2002).

^cThe half-life of a drug is the amount of time required for the plasma drug concentration to decrease by one-half; half-life can be used to determine the appropriate dosing interval (Hardman JG, Limbird LE, Gilman AG (eds.): *Goodman and Gilman's The Pharmacological Basis of Therapeutics*, 10th ed. New York, McGraw-Hill Professional, 2001). The half-life of a drug does not include the half-life of its active metabolites.

TABLE 2. Choice of Medication in the Acute Phase of Schizophrenia

Patient Profile	Consider Medication From			
	Group 1: First-Generation Agents	Group 2: Risperidone, Olanzapine, Quetiapine, Ziprasidone, or Aripiprazole	Group 3: Clozapine	Group 4: Long-Acting Injectable Antipsychotic Agents
First episode		Yes		
Persistent suicidal ideation or behavior			Yes	
Persistent hostility and aggressive behavior			Yes	
Tardive dyskinesia		Yes; all group 2 drugs may not be equal in their lower or no tardive dyskinesia liability	Yes	
History of sensitivity to extrapyramidal side effects		Yes, except higher doses of risperidone		
History of sensitivity to prolactin elevation		Yes, except risperidone		
History of sensitivity to weight gain, hyperglycemia, or hyperlipidemia		Ziprasidone or aripiprazole		
Repeated nonadherence to pharmacological treatment				Yes

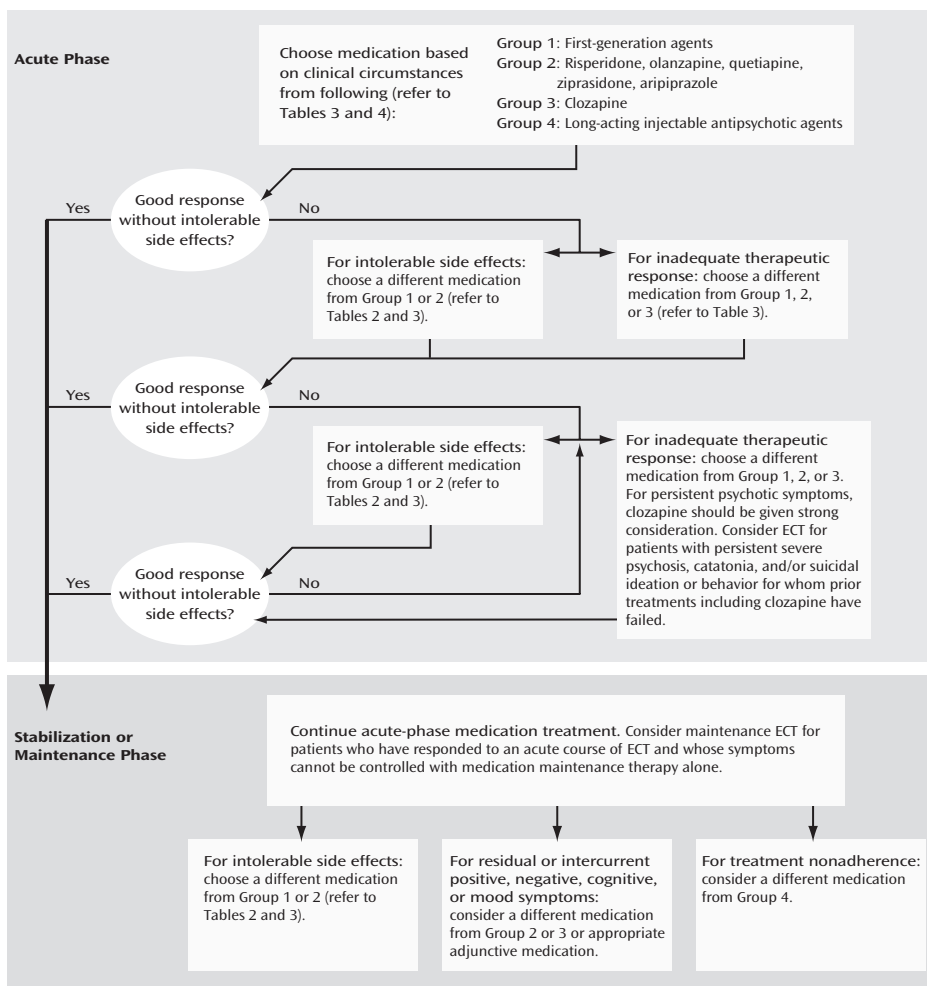
FIGURE 1. Somatic Treatment of Schizophrenia

TABLE 3. Selected Side Effects of Commonly Used Antipsychotic Medications

Medication	Extra-pyramidal Side Effects/ Tardive Dyskinesia		Prolactin Elevation	Weight Gain	Glucose Abnormalities	Lipid Abnormalities	QTc Prolongation	Sedation	Hypotension	Anti-cholinergic Side Effects
	Dyskinesia	Tardive								
Thioridazine	+	++	++	+	+?	+?	+++	++	++	++
Perphenazine	++	++	++	+	+?	+?	0	+	+	0
Haloperidol	+++	+++	+++	+	0	0	0	++	0	0
Clozapine ^a	0 ^b	0	0	+++	+++	+++	0	+++	+++	+++
Risperidone	+	+++	+++	++	++	++	+	+	+	0
Olanzapine	0 ^b	0	0	+++	+++	+++	0	+	+	++
Quetiapine ^c	0 ^b	0	0	++	++	++	0	++	++	0
Ziprasidone	0 ^b	+	+	0	0	0	++	0	0	0
Aripiprazole ^d	0 ^b	0	0	0	0	0	0	+	0	0

0 = No risk or rarely causes side effects at therapeutic dose. + = Mild or occasionally causes side effects at therapeutic dose. ++ = Sometimes causes side effects at therapeutic dose. +++ = Frequently causes side effects at therapeutic dose. ? = Data too limited to rate with confidence.

^aAlso causes agranulocytosis, seizures, and myocarditis.

^bPossible exception of akathisia.

^cAlso carries warning about potential development of cataracts.

^dAlso causes nausea and headache.

Source. Adapted from Tandon R: "Antipsychotic Agents," in *Current Psychotherapeutic Drugs*, Second Edition. Edited by Quitkin FM, Adams DC, Bowden CL, et al. Philadelphia, PA, Current Medicine, 1998, pp. 120–154, with permission of Current Medicine, Inc.

3. Use of Antipsychotic Medications in the Acute Phase (continued)

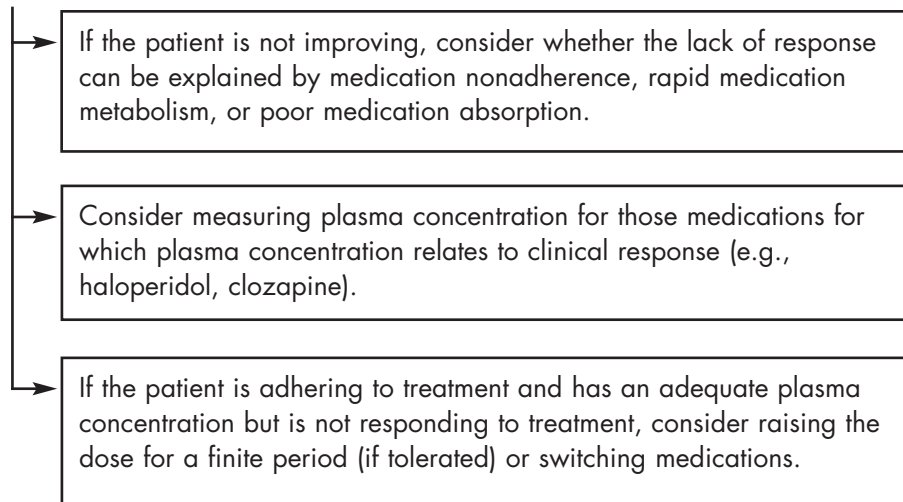
→ Consider second-generation antipsychotics as first-line medications because of the decreased risk for extrapyramidal side effects and tardive dyskinesia.

- For patients who have had prior treatment success or who prefer first-generation agents, these medications are useful and for specific patients may be the first choice.
- With the possible exception of clozapine for patients with treatment-resistant symptoms, antipsychotics generally have similar efficacy in treating positive symptoms.
- Second-generation antipsychotics may have superior efficacy in treating global psychopathology and cognitive, negative, and mood symptoms.

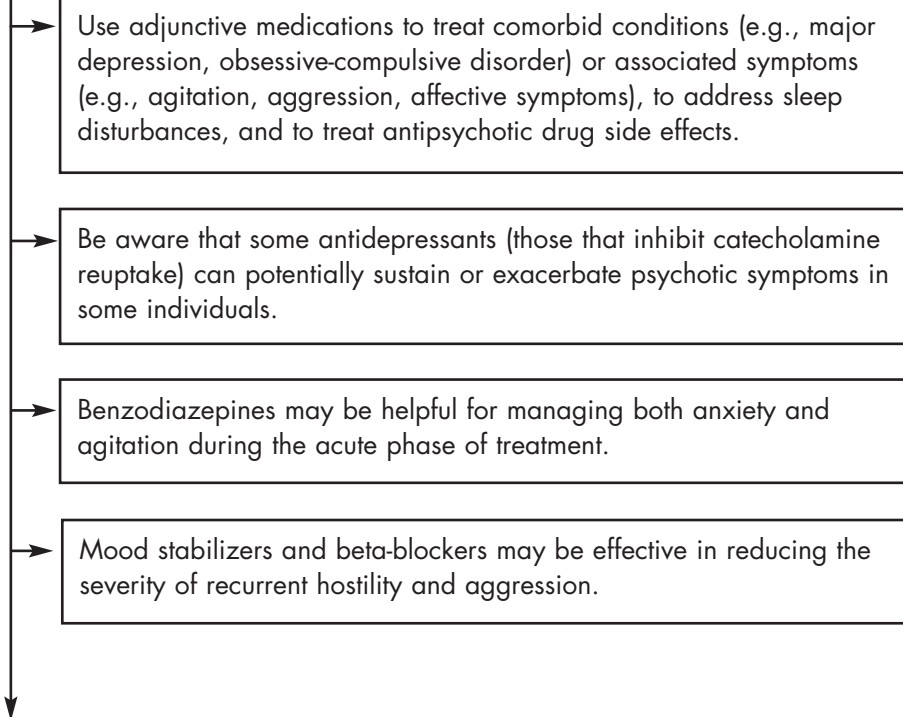
→ Consider long-acting injectable antipsychotic medication for patients with recurrent relapses related to partial or full nonadherence. The oral form of the same medication (e.g., fluphenazine, haloperidol, and risperidone) is the logical choice for initial treatment.

→ Titrate as quickly as tolerated to the target therapeutic dose (sedation, orthostatic hypotension, and tachycardia are generally the side effects that limit the rate of increase), and **monitor clinical status for at least 2 to 4 weeks.**

- The optimal dose of first-generation antipsychotics is, for most patients, at the "extrapyramidal symptom (EPS) threshold," or the dose at which minimal rigidity is detectable on physical examination.
 - For second-generation antipsychotics, target dose usually falls within the therapeutic dose range specified by the manufacturer and in the package labeling approved by the U.S. Food and Drug Administration.
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4. Use of Adjunctive Medications in the Acute Phase



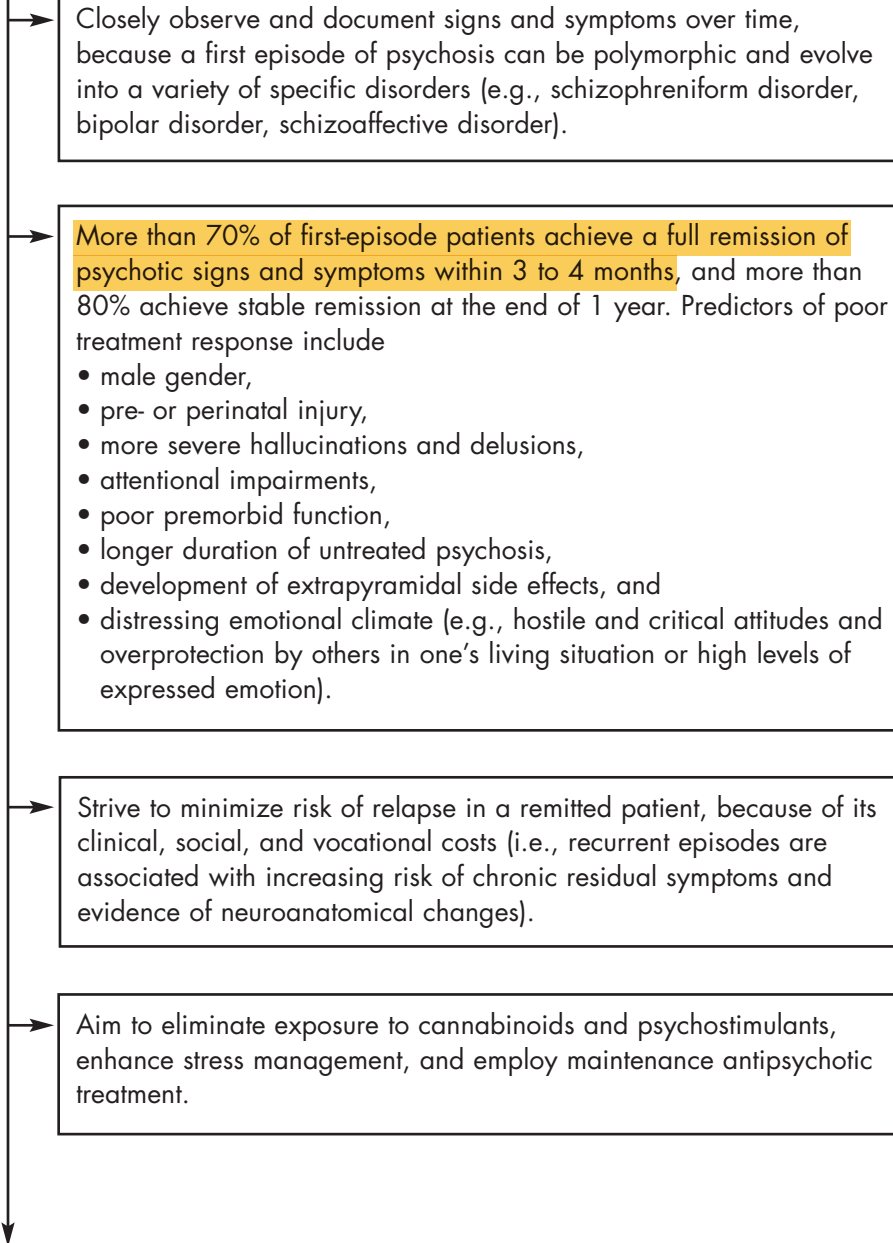
4. Use of Adjunctive Medications in the Acute Phase (continued)

- Consider the following factors when deciding on the prophylactic use of medications to treat extrapyramidal side effects:
 - Propensity of the antipsychotic medication to cause extrapyramidal symptoms (Table 3, p. 133)
 - Patient's preferences
 - Patient's prior history of extrapyramidal symptoms
 - Other risk factors for extrapyramidal symptoms (especially risk factors for dystonia)
 - Risk factors for and potential consequences of anticholinergic side effects
- Other potential strategies for treating extrapyramidal symptoms include lowering the dose of the antipsychotic medication or switching to a different antipsychotic medication.

5. Use of ECT and Other Somatic Therapies in the Acute Phase

- Consider adding ECT to antipsychotic treatment for individuals with schizophrenia or schizoaffective disorder who have persistent severe psychosis and/or suicidal ideation or behaviors and for whom prior treatments, including clozapine, have failed.
- Also consider ECT for individuals with prominent catatonic features that have not responded to an acute trial of lorazepam (e.g., 1 to 2 mg i.v. or i.m. or 2 to 4 mg p.o., repeated as needed over 48 to 72 hours).
- For patients with schizophrenia and comorbid depression, ECT may also be beneficial if depressive symptoms are resistant to treatment or if features such as inanition or suicidal ideation or behavior, which necessitate a rapid response to treatment, are present.

6. Special Issues in Treatment of First-Episode Patients



6. Special Issues in Treatment of First-Episode Patients (continued)

→ Discuss candidly the high risk of relapse and factors that may minimize relapse risk. Prudent treatment options include 1) indefinite antipsychotic maintenance medication and 2) medication discontinuation with close follow-up and a plan of antipsychotic reinstitution with symptom recurrence.

C. Stabilization Phase

→ **Goals of treatment**

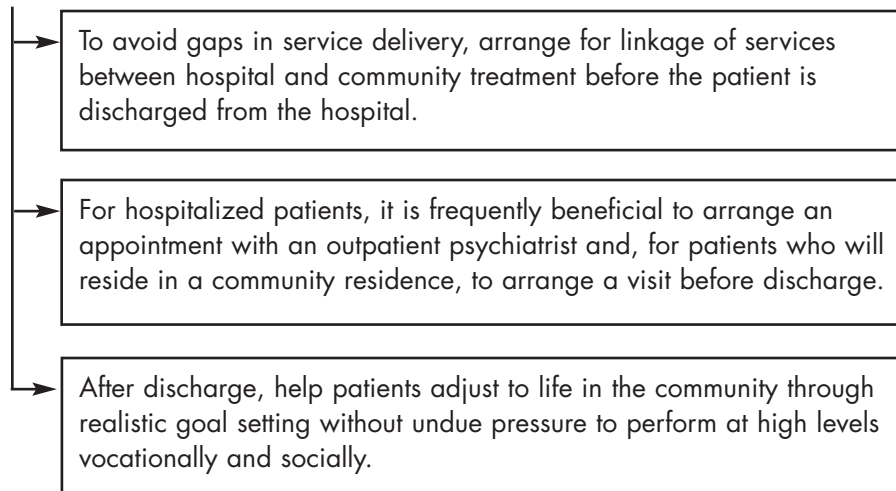
- Minimize stress on the patient and provide support to minimize the likelihood of relapse.
- Enhance the patient's adaptation to life in the community.
- Facilitate continued reduction in symptoms and consolidation of remission, and promote the process of recovery.

→ If the patient has achieved an adequate therapeutic response with minimal side effects, monitor response to the same medication and dose for the next 6 months.

→ Assess adverse side effects continuing from the acute phase, and adjust pharmacotherapy accordingly to minimize them.

→ Continue with supportive psychotherapeutic interventions.

→ Begin education for the patient (and continue education for family members) about the course and outcome of the illness and emphasize the importance of treatment adherence.

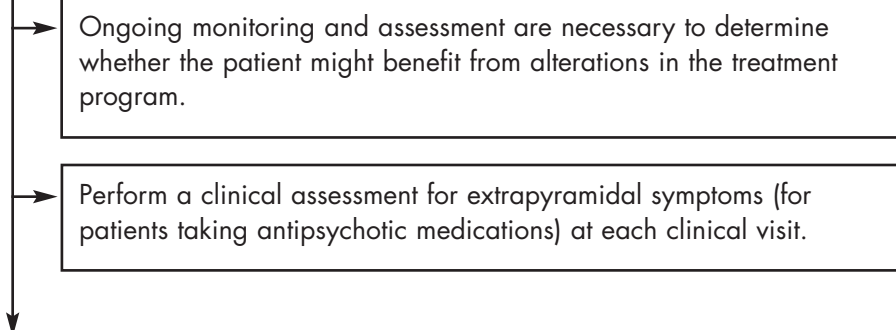


D. Stable Phase

Goals of treatment

- Ensure that symptom remission or control is sustained.
- Maintain or improve the patient's level of functioning and quality of life.
- Effectively treat increases in symptoms or relapses.
- Continue to monitor for adverse treatment effects.

1. Assessment in the Stable Phase



1. Assessment in the Stable Phase (*continued*)

- Perform a clinical assessment for abnormal involuntary movements every 6 months for patients taking first-generation antipsychotics and every 12 months for patients taking second-generation antipsychotics. For patients at increased risk (e.g., elderly patients), assessments should be made every 3 months and 6 months with treatment using first-generation and second-generation antipsychotics, respectively.
- Monitor the patient's weight and BMI at each visit for 6 months and quarterly thereafter. For patients with BMI in the overweight (25 to 29.9 kg/m²) or obese (≥30 kg/m²) range, routinely monitor for obesity-related health problems (e.g., blood pressure, serum lipids, clinical symptoms of diabetes).
- Monitor fasting blood glucose or hemoglobin A1c at 4 months and then annually, and monitor other blood chemistries (e.g., electrolytes; renal, liver, and thyroid function) annually or as clinically indicated; consider drug toxicology screen if clinically indicated.
- Depending on the specific medication being prescribed, consider other assessments, including vital signs, CBC, ECG, screening for symptoms of hyperprolactinemia, and ocular examination.
- If the patient agrees, maintain strong ties with individuals who are likely to notice any resurgence of symptoms and the occurrence of life stresses and events.

2. Psychosocial Treatments in the Stable Phase

- Select appropriate psychosocial treatments based on the circumstances of the individual patient's needs and social context.
- Psychosocial treatments with demonstrated efficacy include
 - family interventions,
 - supported employment,
 - assertive community treatment,
 - social skills training, and
 - cognitive behaviorally oriented psychotherapy.

3. Use of Antipsychotic Medications in the Stable Phase

- Antipsychotics can reduce the risk of relapse in the stable phase of illness to less than 30% per year.
- For most patients treated with first-generation antipsychotics, clinicians should prescribe a dose close to the "EPS threshold" (i.e., the dose that will induce extrapyramidal side effects with minimal rigidity detectable on physical examination).
- Second-generation antipsychotics can generally be administered at doses that are therapeutic but that will not induce extrapyramidal side effects.
- Weigh advantages of decreasing antipsychotics to the "minimal effective dose" against a somewhat greater risk of relapse and more frequent exacerbations of schizophrenia symptoms.
- Evaluate whether residual negative symptoms are in fact secondary to a parkinsonian syndrome or an untreated major depressive syndrome, and treat accordingly.

4. Use of Adjunctive Medications in the Stable Phase

→ Add other psychoactive medication to antipsychotic medications in the stable phase to treat comorbid conditions, aggression, anxiety, or other mood symptoms; to augment the antipsychotic effects of the primary drug; and to treat side effects.

5. Use of ECT in the Stable Phase

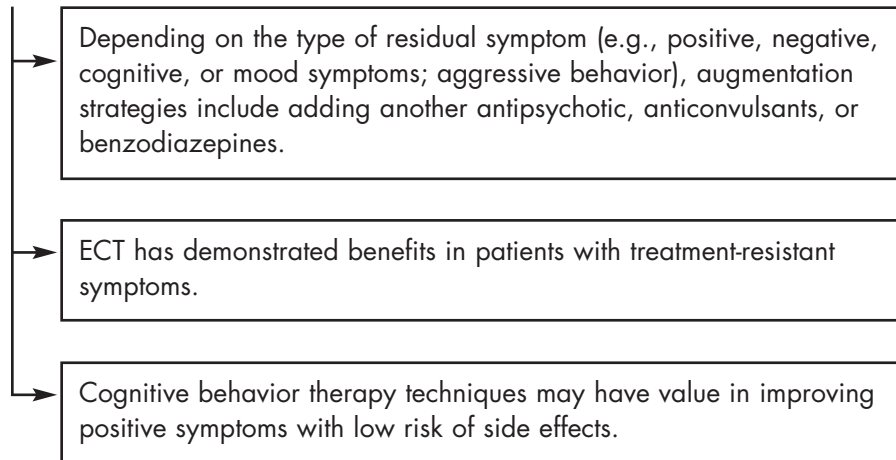
→ Maintenance ECT may be helpful for some patients who have responded to acute treatment with ECT but for whom pharmacologic prophylaxis alone has been ineffective or cannot be tolerated.

6. Encourage the Patient and Family to Use Self-Help Treatment Organizations

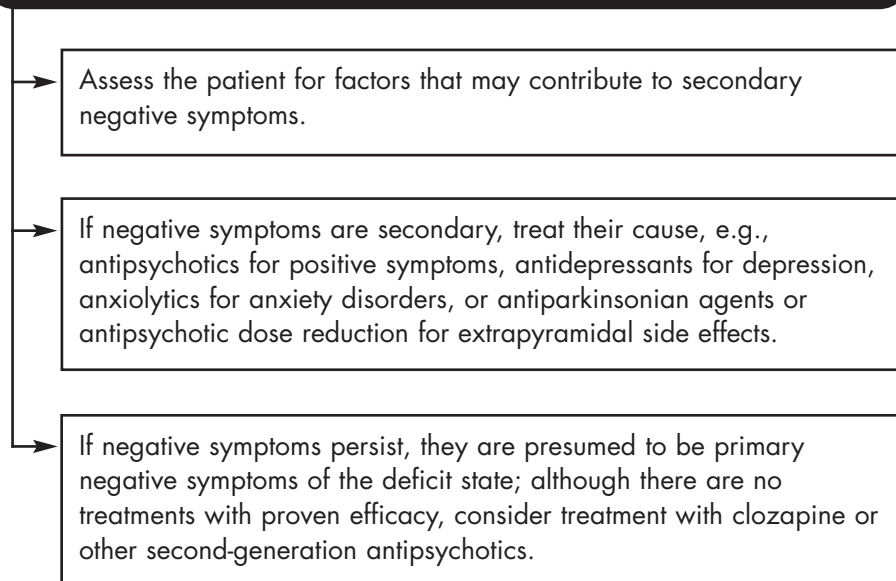
E. Special Issues in Caring for Patients With Treatment-Resistant Illness

→ Carefully evaluate whether the patient has had an adequate trial of an antipsychotic, including whether the dose was adequate and whether the patient was taking the medication as prescribed.

→ Consider a trial of clozapine for a patient who has had what is considered a clinically inadequate response to two antipsychotics (at least one of which was a second-generation antipsychotic) and for a patient with persistent suicidal ideation or behavior that has not responded to other treatments.



F. Treatment of Deficit Symptoms



G. Choice of Treatment Setting or Housing

→ Indications for hospitalization usually include the patient's being considered to pose a serious threat of harm to self or others or being unable to care for self and needing constant supervision or support.

→ Other possible indications for hospitalization include general medical or psychiatric problems that make outpatient treatment unsafe or ineffective.

→ Legal proceedings to achieve involuntary hospitalization are indicated when patients decline voluntary status and hospitalization is clearly warranted.

→ Alternative treatment settings such as day or partial hospitalization, home care, family crisis therapy, crisis residential care, and assertive community treatment should be considered for patients who do not need formal hospitalization for their acute episodes but require more intensive services than can be expected in a typical outpatient setting.

→ Patients may be moved from one level of care to another on the basis of the factors described in Table 4 (p. 145).

TABLE 4. Factors Affecting Choice of Treatment Setting or Housing

Availability of the setting or housing

Patient's clinical condition

- Need for protection from harm to self or others
- Need for external structure and support
- Ability to cooperate with treatment

Patient's and family's preference

Requirements of the treatment plan

- Need for a particular treatment or a particular intensity of treatment that may be available only in certain settings
- Need for a specific treatment for a comorbid psychiatric or other general medical condition

Characteristics of the setting

- Degrees of support, structure, and restrictiveness
- Ability to protect patient from harm to self or others
- Availability of different treatment capacities, including general medical care and rehabilitation services
- Availability of psychosocial supports to facilitate the patient's receipt of treatment and to provide critical information to the psychiatrist about the patient's clinical status and response to treatments
- Capacity to care for severely agitated or psychotic patients
- Hours of operation
- Overall milieu and treatment philosophy

Patient's current environment or circumstances

- Family functioning
- Available social supports

