PRACTICE GUIDELINE FOR THE
Treatment of Patients With Schizophrenia
Second Edition

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Originally published in February 2004. This guideline is more than 5 years old and has not yet been updated to ensure that it reflects current knowledge and practice. In accordance with national standards, including those of the Agency for Healthcare Research and Quality's National Guideline Clearinghouse (http://www.guideline.gov/), this guideline can no longer be assumed to be current.

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CONTENTS

STATEMENT OF INTENT

The American Psychiatric Association (APA) Practice Guidelines 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.

This practice guideline has been developed by psychiatrists who are in active clinical practice. In addition, some contributors are primarily involved in research or other academic endeavors. It is possible that through such activities some contributors, including work group members and reviewers, have received income related to treatments discussed in this guideline. A number of mechanisms are in place to minimize the potential for producing biased recommendations due to conflicts of interest. Work group members are selected on the basis of their expertise and integrity. Any work group member or reviewer who has a potential conflict of interest that may bias (or appear to bias) his or her work is asked to disclose this to the Steering Committee on Practice Guidelines and the work group. Iterative guideline drafts are reviewed by the Steering Committee, other experts, allied organizations, APA members, and the APA Assembly and Board of Trustees; substantial revisions address or integrate the comments of these multiple reviewers. The development of the APA practice guidelines is not financially supported by any commercial organization.

More detail about mechanisms in place to minimize bias is provided in a document available from the APA Department of Quality Improvement and Psychiatric Services, "APA Guideline Development Process."

This practice guideline was approved in December 2003 and published in February 2004.

GUIDE TO USING THIS PRACTICE GUIDELINE

The *Practice Guideline for the Treatment of Patients With Schizophrenia, Second Edition,* consists of three parts (Parts A, B, and C) and many sections, not all of which will be equally useful for all readers. The following guide is designed to help readers find the sections that will be most useful to them.

Part A, "Treatment Recommendations for Patients With Schizophrenia," is published as a supplement to the *American Journal of Psychiatry* and contains general and specific treatment recommendations. Section I summarizes the key recommendations of the guideline and codes each recommendation according to the degree of clinical confidence with which the recommendation is made. Section II is a guide to the formulation and implementation of a treatment plan for the individual patient. Section II.F, "Clinical Features Influencing the Treatment Plan," discusses a range of clinical considerations that could alter the general recommendations discussed in Section II. Section III describes treatment settings and housing options and provides guidance on choice of setting.

Part B, "Background Information and Review of Available Evidence," and Part C, "Future Research Directions," are not included in the *American Journal of Psychiatry* supplement but are provided with Part A in the complete guideline, which is available in print format from American Psychiatric Publishing, Inc., and online through the American Psychiatric Association (http://www.psych.org). Part B provides an overview of schizophrenia, including general information on its natural history, course, and epidemiology. It also provides a structured review and synthesis of the evidence that underlies the recommendations made in Part A. Part C draws from the previous sections and summarizes areas for which more research data are needed to guide clinical decisions.

To share feedback on this or other published APA practice guidelines, a form is available at http://www.psych.org/psych_pract/pg/reviewform.cfm.

DEVELOPMENT PROCESS

This practice guideline was developed under the auspices of the Steering Committee on Practice Guidelines. The development process is detailed in a document available from the APA Department of Quality Improvement and Psychiatric Services: the "APA Guideline Development Process." Key features of this process include the following:

- A comprehensive literature review.
- Development of evidence tables.
- Initial drafting of the guideline by a work group that included psychiatrists with clinical and research expertise in schizophrenia.
- Production of multiple revised drafts with widespread review; four organizations and 62 individuals submitted significant comments.
- Approval by the APA Assembly and Board of Trustees.
- Planned revisions at regular intervals.

Relevant literature was identified through a computerized search of PubMed for the period from 1994 to 2002. Using the keywords schizophrenia OR schizoaffective, a total of 20,009 citations were found. Limiting the search by using the ke words antipsychotic agents, antipsychotic, tranquilizing agents, aripiprazole, olanzapine, ziprasidone, quetiapine, risperidone, clozapine, glycine, beta receptor blockers, antidepressive agents, antidepressant, divalproex, valproic acid, lithium, carbamazepine, benzodiazepines, electroconvulsive therapy, community treatment, psychoeducation, family education, skills training, social support, rehabilitation, case management, community support, supported employment, sheltered workshop, family therapy, family intervention, psychosocial adjustment, cognitive behavior, cognitive training, cognitive therapy, counseling, psychotherapy, group therapy, interpersonal therapy, individual therapy, first break, first episode, new onset, early treatment, and early detection resulted in 8,609 citations. After limiting these references to clinical trials and meta-analyses published in English that included abstracts, 1,272 articles were screened by using title and abstract information. The Cochrane Database of Systematic Reviews was also searched by using the keyword schizophrenia. Additional, less formal literature searches were conducted by APA staff and individual members of the work group on schizophrenia. Sources of funding were considered when the work group reviewed the literature but are not identified in this document. When reading source articles referenced in this guideline, readers are advised to consider the sources of funding for the studies.

This document represents a synthesis of current scientific knowledge and rational clinical practice on the treatment of patients with schizophrenia. It strives to be as free as possible of bias toward any theoretical approach to treatment. In order for the reader to appreciate the evidence base behind the guideline recommendations and the weight that should be given to each recommendation, the summary of treatment recommendations is keyed according to the level of confidence with which each recommendation is made. Each rating of clinical confidence considers the strength of the available evidence and is based on the best available data. When evidence is limited, the level of confidence also incorporates clinical consensus with regard to a particular clinical decision. In the listing of cited references, each reference is followed by a letter code in brackets that indicates the nature of the supporting evidence.

PART A:
TREATMENT RECOMMENDATIONS FOR PATIENTS WITH SCHIZOPHRENIA

I. EXECUTIVE SUMMARY

€ A. CODING SYSTEM

Each recommendation is identified as falling into one of three categories of endorsement, indicated by a bracketed Roman numeral following the statement. The three categories represent varying levels of clinical confidence regarding the recommendation:

[I] Recommended with substantial clinical confidence.
[II] Recommended with moderate clinical confidence.
[III] May be recommended on the basis of individual circumstances.

€ B. FORMULATION AND IMPLEMENTATION OF A TREATMENT PLAN

Because schizophrenia is a chronic illness that influences virtually all aspects of life of affected persons, treatment planning has three goals: 1) reduce or eliminate symptoms, 2) maximize quality of life and adaptive functioning, and 3) promote and maintain recovery from the debilitating effects of illness to the maximum extent possible. Accurate diagnosis has enormous implications for short- and long-term treatment planning, and it is essential to note that diagnosis is a process rather than a one-time event. As new information becomes available about the patient and his or her symptoms, the patient's diagnosis should be reevaluated, and, if necessary, the treatment plan changed.

Once a diagnosis has been established, it is critical to identify the targets of each treatment, to have outcome measures that gauge the effect of treatment, and to have realistic expectations about the degrees of improvement that constitute successful treatment [I]. Targets of treatment, and hence of assessment, may include positive and negative symptoms, depression, suicidal ideation and behaviors, substance use disorders, medical comorbidities, posttraumatic stress disorder (PTSD), and a range of potential community adjustment problems, including homelessness, social isolation, unemployment, victimization, and involvement in the criminal justice system [I].

After the initial assessment of the patient's diagnosis and clinical and psychosocial circumstances, a treatment plan must be formulated and implemented. This formulation involves the selection of the treatment modalities, the specific type(s) of treatment, and the treatment setting. Periodic reevaluation of the diagnosis and the treatment plan is essential to good clinical practice and should be iterative and evolve over the course of the patient's association with the clinician [I].

€ C. ESTABLISHING A THERAPEUTIC ALLIANCE

A supportive therapeutic alliance allows the psychiatrist to gain essential information about the patient and allows the patient to develop trust in the psychiatrist and a desire to cooperate with treatment. Identifying the patient's goals and aspirations and relating these to treatment outcomes fosters the therapeutic relationship as well as treatment adherence [II]. The clinician may also identify practical barriers to the patient's ability to participate in treatment, such as cognitive impairments or disorganization and inadequate social resources. Engagement of the family and other significant support persons, with the patient's permission, is recommended to further strengthen the therapeutic effort [I]. The social circumstances of the patient can have profound effects on adherence and response to treatment. Living situation, family involvement, sources and amount of income, legal status, and relationships with significant others (including children) are all areas that may be periodically explored by mental health care clinicians [II]. The psychiatrist can work with team members, the patient, and the family to ensure that such services are coordinated and that referrals for additional services are made when appropriate. The family's needs can be addressed and an alliance with family members can be facilitated by providing families with information about community resources and about patient and family organizations such as the National Alliance for the Mentally Ill (NAMI) [II].

Many patients with schizophrenia require, and should receive, a variety of treatments, often from multiple clinicians. It is therefore incumbent on clinicians to coordinate their work and prioritize their efforts. Because an accurate history of past and current treatments and responses to them is a key ingredient to treatment planning, excellent documentation is paramount [I]. Especially critical, for example, is information about prior treatment efforts and clinical response.

€ D. ACUTE PHASE TREATMENT

The goals of treatment during the acute phase of treatment, defined by an acute psychotic episode, are to 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, and connect the patient with appropriate aftercare in the community. Efforts to engage and collaborate with family members and other natural caregivers are often successful during the crisis of an acute psychotic episode, whether it is the first episode or a relapse, and are strongly recommended [I]. Family members are often under significant stress during this time. Also, family members and other caregivers are often needed to provide support to the patient while he or she is recovering from an acute episode.

It is recommended that every patient have as thorough an initial evaluation as his or her clinical status allows, including complete psychiatric and general medical histories and physical and mental status examinations [I]. Interviews of family members or other persons knowledgeable about the patient may be conducted routinely, unless the patient refuses to grant permission, especially since many patients are unable to provide a reliable history at the first interview [I]. The most common contributors to symptom relapse are antipsychotic medication nonadherence, substance use, and stressful life events, although relapses are not uncommon as a result of the natural course of the illness despite continuing treatment. If nonadherence is suspected, it is recommended that the reasons for it be evaluated and considered in the treatment plan. General medical health as well as medical conditions that could contribute to symptom exacerbation can be evaluated by medical history, physical and neurological examination, and appropriate laboratory, electrophysiological, and radiological assessments [I]. Measurement of body weight and vital signs (heart rate, blood pressure, temperature) is also recommended [II]. Other laboratory

tests to be considered to evaluate health status include a CBC; measurements of blood electrolytes, glucose, cholesterol, and triglycerides; tests of liver, renal, and thyroid function; a syphilis test; and when indicated and permissible, determination of HIV status and a test for hepatitis C [II]. Routine evaluation of substance use with a toxicology screen is also recommended as part of the medical evaluation [I]. A pregnancy test should be strongly considered for women with childbearing potential [II]. In patients for whom the clinical picture is unclear or where there are abnormal findings from a routine examination, more detailed studies (e.g., screening for heavy metal toxins, EEG, magnetic resonance imaging [MRI] scan, or computed tomography [CT] scan) may be indicated [II].

It is important to pay special attention to the presence of suicidal potential and the presence of command hallucinations and take precautions whenever there is any question about a patient's suicidal intent, since prior suicide attempts, current depressed mood, and suicidal ideation can be predictive of a subsequent suicide attempt in schizophrenia [I]. Similar evaluations are recommended in considering the likelihood of dangerous or aggressive behavior and whether the person will harm someone else or engage in other forms of violence [I].

It is recommended that pharmacological treatment be initiated promptly, provided it will not interfere with diagnostic assessment, because acute psychotic exacerbations are associated with emotional distress, disruption to the patient's life, and a substantial risk of dangerous behaviors to self, others, or property [I]. Before the patient begins treatment with antipsychotic medication, it is suggested that the treating physician, as is feasible, discuss the potential risks and benefits of the medication with the patient [I]. The selection of an antipsychotic medication is frequently guided by the patient's previous experience with antipsychotics, including the degree of symptom response, past experience of side effects, and preferred route of medication administration. In choosing among these medications, the psychiatrist may consider the patient's past responses to treatment, the medication's side effect profile (including subjective responses, such as a dysphoric response to a medication), the patient's preferences for a particular medication based on past experience, the intended route of administration, the presence of comorbid medical conditions, and potential interactions with other prescribed medications [I]. Finally, while most patients prefer oral medication, patients with recurrent relapses related to nonadherence are candidates for a long-acting injectable antipsychotic medication, as are patients who prefer this mode of administration [II].

The recommended dose is that which is both effective and not likely to cause side effects that are subjectively difficult to tolerate, since the experience of unpleasant side effects may affect long-term adherence [I]. The dose may be titrated as quickly as tolerated to the target therapeutic dose of the antipsychotic medication, and unless there is evidence that the patient is having uncomfortable side effects, monitoring of the patient's clinical status for 2–4 weeks is warranted to evaluate the patient's response to the treatment [II]. During these weeks it is often important for physicians to be patient and avoid the temptation to prematurely escalate the dose for patients who are responding slowly [I]. If the patient is not improving, it may be helpful to establish whether the lack of response can be explained by medication nonadherence, rapid medication metabolism, or poor absorption [II].

Adjunctive medications are also commonly prescribed for comorbid conditions in the acute phase. Benzodiazepines may be used to treat catatonia as well as to manage both anxiety and agitation until the antipsychotic has had time to be therapeutically effective [II]. Antidepressants can be considered for treating comorbid major depression or obsessive-compulsive disorder, although vigilance to protect against the risk of exacerbation of psychosis with some antidepressants is important [II]. Mood stabilizers and beta-blockers may be considered for reducing the severity of recurrent hostility and aggression [II]. Careful attention must be paid to potential drug-drug interactions, especially those related to metabolism by cytochrome P450 enzymes [I].

Psychosocial interventions in the acute phase are aimed at reducing overstimulating or stressful relationships, environments, or life events and at promoting relaxation or reduced arousal through simple, clear, coherent communications and expectations; a structured and predictable environment; low performance requirements; and tolerant, nondemanding, supportive relationships with the psychiatrist and other members of the treatment team. Providing information to the patient and the family on the nature and management of the illness that is appropriate to the patient's capacity to assimilate information is recommended [II]. Patients can be encouraged to collaborate with the psychiatrist in selecting and adjusting the medication and other treatments provided [II].

The acute phase is also the best time for the psychiatrist to initiate a relationship with family members, who tend to be particularly concerned about the patient's disorder, disability, and prognosis during the acute phase and during hospitalization [I]. Educational meetings, "survival workshops" that teach the family how to cope with schizophrenia, and referrals to local chapters of patient and family organizations such as NAMI may be helpful and are recommended [III]. Family members may be under considerable stress, particularly if the patient has been exhibiting dangerous or unstable behavior.

€ E. STABILIZATION PHASE

During the stabilization phase, the goals of treatment are to reduce 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 improved with a particular medication regimen, continuation of that regimen and monitoring are recommended for at least 6 months [I]. Premature lowering of dose or discontinuation of medication during this phase may lead to a recurrence of symptoms and possible relapse. It is also critical to assess continuing side effects that may have been present in the acute phase and to adjust pharmacotherapy accordingly to minimize adverse side effects that may otherwise lead to medication nonadherence and relapse [I].

Psychosocial interventions remain supportive but may be less structured and directive than in the acute phase [III]. Education about the course and outcome of the illness and about factors that influence the course and outcome, including treatment adherence, can begin in this phase for patients and continue for family members [II].

It is important that there be no gaps in service delivery, because patients are particularly vulnerable to relapse after an acute episode and need support in resuming their normal life and activities in the community [I]. For hospitalized patients, it is frequently beneficial to arrange an appointment with an outpatient psychiatrist and, for patients who will reside in a community residence, to arrange a visit before discharge [II]. Adjustment to life in the community for patients can be facilitated through realistic goal setting without undue pressure to perform at high levels vocationally and socially, since unduly ambitious expectations can be stressful and can increase the risk of relapse [I]. While it is critical not to place premature demands on the patient regarding engagement in community-based activities and rehabilitation services, it is equally critical to maintain a level of momentum aimed at improving community functioning in order to instill a sense of hope and progress for the patient and family [I].

€ F. STABLE PHASE

The goals of treatment during the stable phase are to ensure that symptom remission or control is sustained, that the patient is maintaining or improving his or her level of functioning and quality of life, that increases in symptoms or relapses are effectively treated, and that monitoring for adverse treatment effects continues. Regular monitoring for adverse effects is recom-

mended [I]. If the patient agrees, it is helpful to maintain strong ties with persons who interact with the patient frequently and would therefore be most likely to notice any resurgence of symptoms and the occurrence of life stresses and events that may increase the risk of relapse or impede continuing functional recovery [II]. For most persons with schizophrenia in the stable phase, psychosocial interventions are recommended as a useful adjunctive treatment to pharmacological treatment and may improve outcomes [I].

Antipsychotic medications substantially reduce the risk of relapse in the stable phase of illness and are strongly recommended [I]. Deciding on the dose of an antipsychotic medication during the stable phase is complicated by the fact that there is no reliable strategy available to identify the minimum effective dose to prevent relapse. For most patients treated with first-generation antipsychotics, a dose is recommended that is around the "extrapyramidal symptom (EPS) threshold" (i.e., the dose that will induce extrapyramidal side effects with minimal rigidity detectable on physical examination), since studies indicate that higher doses are usually not more efficacious and increase the risk of subjectively intolerable side effects [II]. Lower doses of first-generation antipsychotic medications may be associated with improved adherence and better subjective state and perhaps ultimately better functioning. Second-generation antipsychotics can generally be administered at doses that are therapeutic yet well below the "EPS threshold." The advantages of decreasing antipsychotic doses to minimize side effects can be weighed against the disadvantage of a somewhat greater risk of relapse and more frequent exacerbations of schizophrenic symptoms. In general, it is more important to prevent relapse and maintain the stability of the patient [III].

The available antipsychotic medications are associated with differential risk of a variety of side effects, including neurological, metabolic, sexual, endocrine, sedative, and cardiovascular side effects. Monitoring of side effects based on the side effect profile of the prescribed antipsychotic is warranted. During the stable phase of treatment it is important to routinely monitor all patients treated with antipsychotics for extrapyramidal side effects and the development of tardive dyskinesia [I]. Because of the risk of weight gain associated with many antipsychotics, regular measurement of weight and body mass index (BMI) is recommended [I]. Routine monitoring for obesity-related health problems (e.g., high blood pressure, lipid abnormalities, and clinical symptoms of diabetes) and consideration of appropriate interventions are recommended particularly for patients with BMI in the overweight and obese ranges [II]. Clinicians may consider regular monitoring of fasting glucose or hemoglobin A1c levels to detect emerging diabetes, since patients often have multiple risk factors for diabetes, especially patients with obesity [I].

Antipsychotic treatment often results in substantial improvement or even remission of positive symptoms. However, most patients remain functionally impaired because of negative symptoms, cognitive deficits, and limited social function. It is important to evaluate whether residual negative symptoms are in fact secondary to a parkinsonian syndrome or untreated major depression, since interventions are available to address these causes of negative symptoms [II].

Most patients who develop schizophrenia and related psychotic disorders are at very high risk of relapse in the absence of antipsychotic treatment. Unfortunately, there is no reliable indicator to differentiate the minority who will not from the majority who will relapse with drug discontinuation. It is important to discuss with the patient the risks of relapse versus the long-term potential risks of maintenance treatment with the prescribed antipsychotic [I]. If a decision is made to discontinue antipsychotic medication, additional precautions to minimize the risk of a psychotic relapse are warranted. Educating the patient and family members about early signs of relapse, advising them to develop plans for action should these signs appear, and encouraging the patient to attend outpatient visits on a regular basis are warranted [I]. Indefinite maintenance antipsychotic medication is recommended for patients who have had multiple prior episodes or two episodes within 5 years [I]. In patients for whom antipsychotic medications have been prescribed, monitoring for signs and symptoms of impending or actual relapse is recommended [I].

Adjunctive medications are commonly prescribed for comorbid conditions of patients in the stable phase. Comorbid major depression and obsessive-compulsive disorder may respond to antidepressant medications [II]. Mood stabilizers may also address prominent mood lability [II]. Benzodiazepines may be helpful for managing anxiety and insomnia during the stable phase of treatment [II].

In assessing treatment resistance or partial response, it is important to carefully evaluate whether the patient has had an adequate trial of an antipsychotic medication, including whether the dose is adequate and whether the patient has been taking the medication as prescribed. An initial trial of 4–6 weeks generally is needed to determine if the patient will have any symptomatic response, and symptoms can continue to improve over 6 months or even longer periods of antipsychotic treatment [II]. Given clozapine's superior efficacy, a clozapine trial should be considered for a patient who has had no response or partial and suboptimal response to two trials of antipsychotic medication (at least one second-generation agent) or for a patient with persistent suicidal ideation or behavior that has not responded to other treatments [I].

A number of psychosocial treatments have demonstrated effectiveness during the stable phase. They include family intervention [I], supported employment [I], assertive community treatment [I], skills training [II], and cognitive behaviorally oriented psychotherapy [II]. In the same way that psychopharmacological management must be individually tailored to the needs and preferences of the patient, so too should the selection of psychosocial treatments [I]. The selection of appropriate psychosocial treatments is guided by the circumstances of the individual patient's needs and social context [II].

Interventions that educate family members about schizophrenia are needed to provide support and offer training in effective problem solving and communication, reduce symptom relapse, and contribute to improved patient functioning and family well-being [I]. The Program for Assertive Community Treatment (PACT) is a specific model of community-based care that is needed to treat patients who are at high risk for hospital readmission and who cannot be maintained by more usual community-based treatment [I]. Persons with schizophrenia who have residual psychotic symptoms while receiving adequate pharmacotherapy also may be offered cognitive behaviorally oriented psychotherapy [II].

Supported employment is an approach to improve vocational functioning among persons with various types of disabilities, including schizophrenia, and should be made available [I]. The evidence-based supported employment programs that have been found effective include the key elements of services focused on competitive employment, eligibility based on the consumer's choice, rapid job search, integration of rehabilitation and mental health care, attention to the consumer's preferences, and time-unlimited and individualized support.

Social skills training may be helpful in addressing functional impairments with social skills or activities of daily living [II]. The key elements of this intervention include behaviorally based instruction, modeling, corrective feedback, and contingent social reinforcement.

Treatment programs need to combine medications with a range of psychosocial services to reduce the need for crisis-oriented hospitalizations and emergency department visits and enable greater recovery [I].

€ G. OTHER SPECIFIC TREATMENT ISSUES

1. First episode

It is important to treat schizophrenia in its initial episode as soon as possible [II]. When a patient presents with a first-episode psychosis, close observation and documentation of the signs and symptoms over time are important because first episodes of psychosis can be polymorphic and evolve into a variety of specific disorders (e.g., schizophreniform disorder, bipolar disorder, schizoaffective disorder) [I]. Furthermore, in persons who meet the criteria for being prodromally

symptomatic and at risk for psychosis in the near future, careful assessment and frequent monitoring are recommended until symptoms remit spontaneously, evolve into schizophrenia, or evolve into another diagnosable and treatable mental disorder [III]. The majority of first-episode patients are responsive to treatment, with more than 70% achieving remission of psychotic signs and symptoms within 3–4 months and 83% achieving stable remission at the end of 1 year. First-episode patients are generally more sensitive to the therapeutic effects and side effects of medications and often require lower doses than patients with chronic schizophrenia. Minimizing risk of relapse in a remitted patient is a high priority, given the potential clinical, social, and vocational costs of relapse [I]. Family members are especially in need of education and support at the time of the patient's first episode [I].

2. Negative symptoms

Treatment of negative symptoms begins with assessing the patient for syndromes that can cause the appearance of secondary negative symptoms [I]. The treatment of such secondary negative symptoms consists of treating their cause, e.g., antipsychotics for primary positive symptoms, antidepressants for depression, anxiolytics for anxiety disorders, or antiparkinsonian agents or antipsychotic dose reduction for extrapyramidal side effects [III]. If negative symptoms persist, they are presumed to be primary negative symptoms of the deficit state. There are no treatments with proven efficacy for primary negative symptoms.

3. Substance use disorders

Nearly one-half of patients with schizophrenia have comorbid substance use disorders, excluding nicotine abuse/dependence, which itself exceeds 50% in prevalence in this group. The goals of treatment for patients with schizophrenia who also have a substance use disorder are the same as those for treatment of patients with schizophrenia without comorbidity but with the addition of the goals for the treatment of substance use disorders, e.g., harm reduction, abstinence, relapse prevention, and rehabilitation. A comprehensive integrated treatment model is recommended in which the same clinicians or team of clinicians provide treatment for schizophrenia as well as treatment of substance use disorders [III]. This form of treatment features assertive outreach, case management, family interventions, housing, rehabilitation, and pharmacotherapy. It also includes behavioral interventions for those who are trying to attain or maintain abstinence and a stage-wise motivational approach for patients who do not recognize the need for treatment of a substance use disorder.

4. Depression

Depressive symptoms are common at all phases of schizophrenia. A careful differential diagnosis that considers the contributions of side effects of antipsychotic medications, demoralization, the negative symptoms of schizophrenia, and substance intoxication or withdrawal is recommended [I]. Depressive symptoms that occur during the acute psychotic phase usually improve as patients recover from the psychosis. There is also evidence to suggest that depressive symptoms are reduced by antipsychotic treatment, with comparison trials finding that second-generation antipsychotics may have greater efficacy for depressive symptoms than first-generation antipsychotics [II]. Antidepressants may be added as an adjunct to antipsychotics when the depressive symptoms meet the syndromal criteria for major depressive disorder or are severe, causing significant distress or interfering with function [II].

5. Suicidal and aggressive behaviors

Suicide is the leading cause of premature death among patients with schizophrenia. Some risk factors for suicide among patients with schizophrenia are the same as those for the general pop-

ulation: male gender, white race, single marital status, social isolation, unemployment, a family history of suicide, previous suicide attempts, substance use disorders, depression or hopelessness, and a significant recent adverse life event. Specific demographic risk factors for suicide among persons with schizophrenia are young age, high socioeconomic status background, high IQ with a high level of premorbid scholastic achievement, high aspirations and expectations, early age at onset/first hospitalization, a chronic and deteriorating course with many relapses, and greater insight into the illness.

Despite identification of these risk factors, it is not possible to predict whether an individual patient will attempt suicide or die by suicide. It is important to consider suicide risk at all stages of the illness and to perform an initial suicide risk assessment and regular evaluation of suicide risk as part of each patient's psychiatric evaluation [I]. There is evidence to suggest that both first- and second-generation antipsychotic medications may reduce the risk of suicide. However, clozapine is the most extensively studied and has been shown to reduce the rates of suicide [II] and persistent suicidal behavior [I].

During a hospitalization, use of suicide precautions and careful monitoring over time for suicidal patients are essential [I]. Upon discharge, the patient and the family members may be advised to look for warning signs and to initiate specific contingency plans if suicidal ideation recurs [I]. After a recent discharge from the hospital, a higher frequency of outpatient visits is recommended, and the number of visits may need to be increased during times of personal crisis, significant environmental changes, heightened distress, or deepening depression during the course of illness [III].

A minority of patients with schizophrenia have an increased risk for aggressive behavior. The risk for aggressive behavior increases with comorbid alcohol abuse, substance abuse, antisocial personality, or neurological impairment. Identifying risk factors for aggressive behavior and assessment of dangerousness are part of a standard psychiatric evaluation [I].

€ H. TREATMENT SETTINGS AND HOUSING OPTIONS

Patients with schizophrenia may receive care in a variety of settings. In general, patients should be cared for in the least restrictive setting that is likely to be safe and to allow for effective treatment [I]. 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 [I]. Other possible indications for hospitalization include general medical or psychiatric problems that make outpatient treatment unsafe or ineffective [III] or new onset of psychosis [III]. Efforts should be made to hospitalize such patients voluntarily [I].

Treatment programs that emphasize highly structured behavioral techniques, including a token economy, point systems, and skills training that can improve patients' functioning, are recommended for patients with treatment-resistant schizophrenia who require long-term hospitalization [I].

When it is uncertain whether the patient needs to be hospitalized, alternative treatment in the community, such as day hospitalization, home care, family crisis therapy, crisis residential care, or assertive community treatment, should be considered [III]. Day hospitalization can be used as an immediate alternative to inpatient care for acutely psychotic patients or used to continue stabilization after a brief hospital stay [III].

Day treatment programs can be used to provide ongoing supportive care for marginally adjusted patients with schizophrenia in the later part of the stabilization phase and the stable phase of illness, and such programs are usually not time-limited [III]. The goals are to provide structure, support, and treatment to help prevent relapse and to maintain and gradually improve the patient's social functioning [III].

II. FORMULATION AND IMPLEMENTATION OF A TREATMENT PLAN

Because schizophrenia is a chronic illness that affects virtually all aspects of life of affected persons, treatment planning has three goals: 1) reduce or eliminate symptoms, 2) maximize quality of life and adaptive functioning, and 3) enable recovery by assisting patients in attaining personal life goals (e.g., in work, housing, and relationships). For purposes of presentation throughout this guideline, the course of treatment for persons with schizophrenia is divided into three phases: acute, stabilization, and stable. The acute phase begins with a new onset or acute exacerbation of symptoms and spans the period until these symptoms are reduced to a level considered to be the patient's expected "baseline." The stabilization period follows the acute phase and constitutes a time-limited transition to continuing treatment in the stable phase. Combined, the acute and stabilization phases generally span approximately 6 months. The stable phase represents a prolonged period of treatment and rehabilitation during which symptoms are under adequate control and the focus is on improving functioning and recovery. While these distinctions may be somewhat arbitrary, they provide a useful framework for discussion of treatment.

Many of the advances in the treatment of schizophrenia over the past two decades have come from recognition of the complexities of the manifestations and the different stages of the illness. These insights into the multiple components of psychopathology in schizophrenia and into the role of family, social, and other environmental factors in influencing both psychopathology and adaptation have resulted in development of a wide range of treatments that target specific aspects of the illness. Recognition of the different stages of the illness has led to various approaches in treatment planning, treatment selection, and drug dosing. Fragmentation of services and treatments has long been a problem in delivering comprehensive care to persons with schizophrenia. This fragmentation is determined by several factors, including the use of many different treatment settings, the necessary involvement of several professional disciplines, and the use of multiple funding streams, coupled with inadequate insurance coverage and the decline in funding for public and private mental health services, to mention just a few. It is critical, under these circumstances, that there be an overarching treatment plan that serves the short- and long-term needs of the patient and that is periodically modified as clinical circumstances change and new knowledge about treatments becomes available.

€ A. PSYCHIATRIC MANAGEMENT

This section is an overview of key issues in the psychiatric management of patients with schizophrenia. It highlights areas that research has shown to be important in affecting the course of illness and success of treatment. These issues arise in the management of all psychiatric illnesses. This section notes the particular ways in which they occur in the treatment of patients with schizophrenia.

1. Assessing symptoms and establishing a diagnosis

Effective and appropriate treatments are based on accurate, relevant diagnostic and clinical assessments. In the case of schizophrenia, the diagnosis has major implications for short- and long-term treatment planning. (See Part B, Section IV.A, "Clinical Features," for a description of the characteristic symptoms of schizophrenia and the DSM-IV-TR criteria for diagnosis of

the illness.) It is beyond the scope of this guideline to discuss the differential diagnosis of psychotic disorders and their evaluation. However, it is important to note that diagnosis is a process rather than a one-time event. As new information becomes available about the patient and his or her symptoms, the patient's diagnosis should be reevaluated and, if necessary, the treatment plan changed.

Proper diagnosis, while essential, is insufficient to adequately guide treatment of schizophrenia. Treatments are directed at the manifestations and sequelae of schizophrenia. It is critical to identify the targets of each treatment, to have outcome measures that gauge the effect of treatment, and to have realistic expectations about the degrees of improvement that constitute successful treatment. Depression, suicide, homelessness, substance use disorders, medical comorbidities, social isolation, joblessness, criminal victimization, past sexual or physical abuse, and involvement in the criminal justice system are all far more common among persons with schizophrenia, particularly in the chronic stages of the illness, than in the general population. In addition to the core symptoms of schizophrenia, these areas need careful assessment and, as warranted, appropriate interventions.

A number of objective, quantitative rating scales to monitor clinical status in schizophrenia are available, as described in the American Psychiatric Association's (APA's) *Handbook of Psychiatric Measures* (1). They include the Structured Clinical Interview for DSM-IV (2) for establishing diagnosis, the Abnormal Involuntary Movement Scale (3) for monitoring tardive dyskinesia and other abnormal movements, and the Brief Psychiatric Rating Scale (BPRS) (4–6) and the Positive and Negative Syndrome Scale (PANSS) (7) for monitoring psychopathology. Other brief structured assessments are also available (8, 9). There are several reasons that use of rating scales is important. First, rating scales provide a record that documents the patient's response to treatment. This record is of particular value when the treatment is nonstandard (e.g., combination of antipsychotics) or expensive. Second, the ratings can be compared with the patient's, family members', and clinician's impressions of treatment effects and over time can clarify the longitudinal course of the patient's illness. This process can help temper excessive optimism when new treatments are begun and can provide useful information about the actual effects of prior treatments. Third, use of anchored scales with criteria to assess the severity and frequency of symptoms helps patients become more informed self-observers. Finally, use of the rating scales over time ensures that information about the same areas is collected at each administration and helps avoid omission of key elements of information needed to guide treatment.