I. Indications for Using Antipsychotics in Older Patients

Guideline 1: Indications for Antipsychotics[Question 1]

The experts stated that antipsychotics are indicated for disorders with psychotic symptoms, i.e. schizophrenia, mania with psychosis, agitated dementia with delusions, psychotic major depression, and delusional disorder. They suggested that antipsychotics are sometimes indicated for mania without psychosis, delirium, and agitated dementia without delusions. They would not generally recommend antipsychotics in the other conditions we asked about.

(***bold italics*** = indications receiving top ratings from at least 50% of the experts)

Antipsychotics usually indicated	Antipsychotics sometimes indicated	Antipsychotics not generally indicated
Schizophrenia Mania with psychosis Dementia with agitation with delusions Psychotic major depression Delusional disorder	Mania without psychosis Delirium Dementia with agitation without delusions Agitated nonpsychotic major depression* Nonpsychotic major depression with severe anxiety*	Severe nausea and vomiting (e.g., due to chemotherapy) Irritability and hostility in the absence of a major psychiatric syndrome Nonpsychotic major depression without severe anxiety Neuropathic pain Panic disorder Generalized anxiety disorder Hypochondriasis Motion sickness Insomnia/sleep disturbance in the absence of a major psychiatric syndrome or a discrete medical cause

*These disorders were rated lower second line. The use of antipsychotics for these conditions may sometimes be appropriate, especially for patients with refractory depression that has failed to respond to other treatments.

II. Diagnosis, Medication Selection, and Dosing for Specific Indications

Guideline 2: Delirium

2A. Diagnosis of Delirium[Question 2]

The features that the experts consider most important in diagnosing delirium reflect the criteria given in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV).*

(***bold italics*** = features rated "extremely important" by at least 50% of the experts)

Most important discriminating features	Also consider
Disturbance of consciousness (i.e., reduced clarity of awareness of environment) with reduced ability to focus, sustain, or shift attention The disturbance has a fluctuating course (waxes and wanes) during the course of the day The disturbance develops over a short period of time Evidence that the patient has recently used drugs that can cause intoxication or withdrawal delirium Workup identifies a medical illness (e.g., dehydration, urinary tract infection) that could be causing the delirium Change in cognitive function (e.g., disorientation, language disturbance, perceptual disturbance)	The patient has recently been exposed to an environmental toxin that can cause delirium If hallucinations or delusions are present, these symptoms fluctuate and are fragmented and unsystematized History of a dementing disorder

*American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Washington, DC: American Psychiatric Association; 1994

2B. Selecting Antipsychotics for Delirium[Question 14]

There was no consensus among the experts on a first-line antipsychotic for delirium. Risperidone received high second-line ratings at the dosages noted below. We used the mean ± one standard deviation of the experts' write-in responses to generate a dosing range that was then rounded to currently available pill strengths. Quetiapine received lower second-line ratings. Although high-potency conventional antipsychotics and olanzapine also received second-line ratings, there was no consensus on these options.

Preferred	Also consider
(None)	Risperidone 0.75–1.75 mg/day

Guideline 3: Dementia

3A. Identifying Conditions Contributing to Dementia With Agitation[Question 10]

We asked the experts which conditions need to be addressed before intervening with antipsychotic drugs in an agitated older patient with dementia. The experts considered delirium the single most important condition to address (94% first line), followed by agitated depression (88% first line); 60% or more of the experts also gave first-line ratings to pain, dysuria, dyspnea, and abdominal discomfort, and 50% gave first-line ratings to pruritus.

(***bold italics*** = conditions rated "extremely important" by at least 50% of the experts)

Most important conditions to identify and address before intervening with antipsychotic medication	Other important conditions to consider
Delirium Agitated depression	Pain (e.g., from osteoarthritis) Dysuria (e.g., due to infection) or urinary urgency (e.g., due to uninhibited bladder contractions) Dyspnea (e.g., due to cardiac or lung disease) Abdominal discomfort (e.g., due to constipation) Pruritus (severe itching)

3B. Selecting Treatments for Dementia With Agitation[Questions 11 & 12]

The experts' first-line recommendation for treating agitated dementia with delusions was an antipsychotic drug alone; they would also consider combining a mood stabilizer with an antipsychotic. There was no first-line recommendation for treating agitated dementia without delusions; an antipsychotic alone was a high second-line option (rated first line by 60% of the experts); the experts would also consider a mood stabilizer alone (rated first line by 35%).

	Preferred	Also consider
With delusions	An antipsychotic alone	A mood stabilizer plus an antipsychotic
Without delusions	*(None)*	An antipsychotic alone A mood stabilizer alone

3C. Selecting Antipsychotics for Dementia With Agitation[Question 13]

Among antipsychotic drugs, the experts recommended risperidone at dosages noted below as the first-line choice for agitated dementia. Quetiapine and olanzapine were high second-line options.

The survey on which these recommendations were based was completed by the experts at a time when information became available of a potential association between risperidone and cerebrovascular adverse events (CAEs). In October 2002, a letter was sent to physicians in Canada warning about CAEs associated with risperidone (Risperdal). In February 2003, a study by Brodaty et al.* showed that demented patients treated with risperidone had more CAEs than patients treated with placebo. In March 2003, the American FDA included the following information in the WARNINGS section of the risperidone package insert:

> **Cerebrovascular Adverse Events, Including Stroke, in Elderly Patients With Dementia:** Cerebrovascular adverse events (e.g., stroke, transient ischemic attack), including fatalities, were reported in patients (mean age 85 years; range 73–97) in trials of RISPERDAL in elderly patients with dementia-related psychosis. In placebo-controlled trials, there was a significantly higher incidence of cerebrovascular adverse events in patients treated with RISPERDAL compared to patients treated with placebo. RISPERDAL has not been shown to be safe or effective in the treatment of patients with dementia-related psychosis.

The following information is included in the ADVERSE REACTIONS section of the risperidone package insert:

> **Postintroduction Reports:** Adverse events reported since market introduction which were temporally (but not necessarily causally) related to RISPERDAL therapy include: …cerebrovascular disorder, including cerebrovascular accident… A causal relationship with RISPERDAL has not been established.

On April 16, 2003, Janssen Pharmaceutica, L.P., the manufacturer of risperidone, mailed a letter to American physicians informing them of the potential risk for CAEs. Our methods do not permit us to ascertain to what extent the experts who completed this survey were aware of these findings. The survey on which these guidelines are based was sent to experts on February 10, 2003. All surveys were returned after the Brodaty et al. article was published. Of the 48 surveys, 35 were returned before the date on which the letter from Janssen was mailed to U.S. physicians (23 surveys returned in March 2003 and 12 surveys returned between April 1 and April 16). The remaining 13 surveys were returned in the second half of April 2003 or in May 2003. We note that, prior to the mailing of the survey to the experts, the risperidone label, and the labels of other atypical and typical antipsychotic drugs, already included the same level of warning for various other potential adverse effects, such as neuroleptic malignant syndrome, tardive dyskinesia, and cardiac proarrhythmic effects.

Preferred	**Also consider**
Risperidone 0.5–2.0 mg/day	Quetiapine 50–150 mg/day Olanzapine 5.0–7.5 mg/day

*Brodaty H, Ames D, Snowdon J, et al. A randomized placebo-controlled trial of risperidone for the treatment of aggression, agitation, and psychosis of dementia. J Clin Psychiatry 2003;64:134–143.

Guideline 4: Schizophrenia

4A. Diagnosis of Schizophrenia[Question 3]

The experts considered delusions, hallucinations, and a long-term history of psychotic symptoms the most important features in diagnosing schizophrenia in an older patient. Other important features are grossly disorganized behavior and disorganized speech. The experts also gave high second-line ratings to symptoms that are useful in distinguishing schizophrenia from delirium, psychosis related to medications or medical illness, and mood disorders.

Most important discriminating features	Also consider
Delusions Hallucinations Long-term history of psychotic symptoms	Grossly disorganized behavior Disorganized speech Absence of alterations in consciousness or impaired attention Workup rules out a medical illness (e.g., lupus erythematosus) that could be causing the psychotic symptoms No evidence that the patient has recently used drugs (e.g., psychostimulants) that can cause psychotic symptoms Affective flattening (diminished range of emotional expressiveness) The duration of mood symptoms is brief in relation to the total duration of the disturbance Avolition (inability to initiate and persist in goal-directed activities)

4B. Selecting Antipsychotics for Schizophrenia[Question 20]

The experts' first-line recommendation for treating schizophrenia in an older patient was risperidone, followed by quetiapine, olanzapine, and aripiprazole as high second-line options at the dosages noted below. The experts were divided in their ratings of aripiprazole, with 60% giving this agent first-line ratings and 20% third-line ratings, probably reflecting limited experience with this recently introduced agent. There was limited support for the use of ziprasidone, clozapine, and high-potency conventional antipsychotics.

Preferred	Also consider
Risperidone 1.25–3.5 mg/day	Quetiapine 100–300 mg/day Olanzapine 7.5–15 mg/day Aripiprazole 15–30 mg/day*

*The surveys on which these guidelines are based were completed between March and May 2003. Note that aripiprazole was approved November 15, 2002.

Guideline 5: Delusional Disorder

5A. Diagnosis of Delusional Disorder[Question 4]

The features that the experts considered most important in diagnosing delusional disorder reflect the criteria given in the DSM-IV. The experts stressed the importance of accurate differential diagnosis to rule out the effects of medications, medical illness, delirium, schizophrenia, and depression.

Most important discriminating features	**Also consider**
Nonbizarre delusions that have lasted at least 1 month The person does not display disorganized speech or disorganized or bizarre behavior No prominent auditory or visual hallucinations No evidence that the patient has recently used drugs (e.g., psychostimulants) that can cause delusions Aside from the delusions, the person's functioning is not markedly impaired Workup rules out a medical illness (e.g., dementia of the Alzheimer's type) that could be causing the delusions Absence of alterations in consciousness or impaired attention	The person does not have negative symptoms (affective flattening, alogia, avolition) Absence of cognitive impairment Absence of mood symptoms, or mood symptoms of brief duration

5B. Selecting Treatments for Delusional Disorder[Question 24]

An antipsychotic was the only treatment recommended by the experts for delusional disorder.

5C. Selecting Antipsychotics for Delusional Disorder[Question 25]

The experts' first-line recommendation for delusional disorder in an older patient was risperidone, followed by olanzapine and quetiapine as high second-line options at the dosages noted below. There was no consensus on aripiprazole and ziprasidone, while conventional antipsychotics and clozapine were rated third line.

Preferred	**Also consider**
Risperidone 0.75–2.5 mg/day	Olanzapine 5–10 mg/day Quetiapine 50–200 mg/day

Guideline 6: Nonpsychotic Major Depressive Disorder

6A. Diagnosis of Nonpsychotic Major Depressive Disorder[Question 5]

The experts considered depressed mood, most of the day, every day, markedly diminished interest or pleasure in activities, and recurrent thoughts of death or suicidal ideation or behavior the three most important discriminating features in diagnosing nonpsychotic major depression in an older patient. These three symptoms have consistently been endorsed in studies of depression in the elderly and were considered the most important symptoms in diagnosing depression in an older patient by a survey of experts on the treatment of depressive disorders in older patients.*

(***bold italics*** = features rated "extremely important" by at least 50% of the experts)

Most important discriminating features	Also consider
Depressed mood most of the day, every day Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day Recurrent thoughts of death, recurrent suicidal ideation, or a suicide attempt Feelings of worthlessness or excessive or inappropriate guilt nearly every day	Change in sleep patterns (insomnia or hypersomnia) Fatigue or loss of energy nearly every day Psychomotor agitation or retardation nearly every day Significant weight loss (when not dieting) or weight gain or a decrease or increase in appetite nearly every day Diminished ability to think or concentrate or indecisiveness nearly every day Workup rules out a medical illness (e.g., Parkinson's disease) that could be causing the depression The symptoms are not better accounted for by schizoaffective disorder, schizophrenia, or delusional disorder The patient has never had a hypomanic, manic, or mixed episode No evidence that the patient has recently used a drug (e.g., interferon) that can cause depression

*Alexopoulos GS, Katz IR, Reynolds CF, et al. The Expert Consensus Guideline Series: Pharmacotherapy of Depressive Disorders in Older Patients. Postgrad Med Special Report 2001;October:22.

6B. Selecting Treatments for Nonpsychotic Major Depressive Disorder[Question 15]

The experts first-line recommendation for agitated nonpsychotic major depression in an older patient was an antidepressant alone (rated first line by 77%). Second-line options were an antidepressant plus an antipsychotic (44% first line), ECT (31% first line), an antidepressant plus a benzodiazepine (25% first line), and an antidepressant plus a mood stabilizer (23% first line). For nonpsychotic major depression accompanied by severe anxiety, the experts again recommended an antidepressant alone (79% first line). They would also consider adding a benzodiazepine to the antidepressant (51% first line) or using ECT (25% first line).

	Preferred	Also consider
With Agitation	An antidepressant alone	An antipsychotic plus an antidepressant
With Severe Anxiety	An antidepressant alone	A benzodiazepine plus an antidepressant

6C. Selecting Antidepressants for Nonpsychotic Major Depressive Disorder[Question 16]

When asked which specific antidepressants they preferred for the treatment of nonpsychotic major depression in an older patient, the experts recommended a selective serotonin reuptake inhibitor (SSRI) as the first-line choice, followed by venlafaxine and mirtazapine as high second-line options. There was much less support for tricyclic antidepressants, trazodone, and bupropion, while the monoamine oxidase inhibitors received third-line ratings.

	Preferred	**Also consider**
With Agitation	A selective serotonin reuptake inhibitor (SSRI)	Venlafaxine Mirtazapine
With Severe Anxiety	SSRI	Venlafaxine Mirtazapine

6D. Use of Atypical Antipsychotics in Treatment-Resistant Nonpsychotic Major Depressive Disorder[Question 17]

We asked the experts about adding an atypical antipsychotic to an antidepressant in an older patient with treatment-resistant nonpsychotic major depression. We specified that the trials had involved adequate therapeutic doses of antidepressants and were of adequate duration. There was limited support for this strategy; 36% of the experts would add an atypical antipsychotic if a patient had failed adequate trials of two antidepressants.

Guideline 7: Psychotic Major Depressive Disorder

7A. Diagnosis of Psychotic Major Depressive Disorder[Question 5]

To diagnose psychotic major depression in an older patient, the experts required the presence of both delusions and the following three key depressive symptoms: depressed mood, most of the day, every day, markedly diminished interest or pleasure in activities, and recurrent thoughts of death or suicidal ideation or behavior (see Guideline 6A).

Most important discriminating features	Also consider
Depressed mood most of the day, every day Delusions that occur only when the depressive symptoms are present Recurrent thoughts of death, recurrent suicidal ideation, or a suicide attempt Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day A previous episode of psychotic depression Feelings of worthlessness or excessive or inappropriate guilt nearly every day The symptoms are not better accounted for by schizoaffective disorder, schizophrenia, or delusional disorder Psychomotor agitation or retardation nearly every day Change in sleep patterns (insomnia or hypersomnia)	Significant weight loss (when not dieting) or weight gain or a decrease or increase in appetite nearly every day Diminished ability to think or concentrate or indecisiveness nearly every day Fatigue or loss of energy nearly every day Workup rules out a medical illness (e.g., Parkinson's disease) that could be causing the depression The patient has never had a hypomanic, manic, or mixed episode No evidence that the patient has recently used a drug (e.g., interferon) that can cause depression

7B. Selecting Treatments for Psychotic Major Depressive Disorder[Question 18]

The treatment of choice for psychotic major depression in an older patient was an antipsychotic plus an antidepressant, which was rated first line by 98% of the experts. Electroconvulsive therapy (ECT) is another first-line option (rated first line by 71%). Other second-line options—an antidepressant alone or a mood stabilizer plus an antipsychotic—received only limited support.

(***bold italics*** = treatment of choice)

Preferred	Also consider
An antipsychotic plus an antidepressant Electroconvulsive therapy (ECT)	*(None)*

7C. Selecting Antipsychotics to Treat Psychotic Major Depressive Disorder[Question 19]

Risperidone at the dosages shown below was the first-line option for use in combination with an antidepressant for psychotic major depression (rated first line by 91% of the experts). Olanzapine and quetiapine were high second-line options (rated first line by approximately 70% of the experts). There was no consensus on aripiprazole or ziprasidone.

Preferred	Also consider
Risperidone 0.75–2.25 mg/day	Olanzapine 5–10 mg/day Quetiapine 50–200 mg/day

Guideline 8: Mania (Bipolar I Disorder)

8A. Diagnosis of Nonpsychotic Mania[Question 6]

The experts considered elevated, expansive, or irritable mood that persists for at least 1 week the single most important discriminating feature in diagnosing nonpsychotic mania in an older patient. The other features they endorsed agree closely with the DSM-IV criteria for a manic episode.

(***bold italics*** = features rated "extremely important" by at least 50% of the experts)

Most important discriminating features	Also consider
Elevated, expansive, or irritable mood that persists for at least 1 week Inflated self-esteem or grandiosity for at least 1 week Flight of ideas or subjective experience that thoughts are racing, occurring frequently for at least 1 week Excessive involvement in pleasurable activities that have a high potential for negative consequences (e.g., buying sprees, foolish business investments) Decreased need for sleep for at least 1 week	Workup rules out a medical illness (e.g., multiple sclerosis, stroke) that could be causing the manic symptoms No evidence that the patient has recently used a drug (e.g., cocaine, antidepressant medication) that can cause manic symptoms The symptoms are not better accounted for by schizoaffective disorder, schizophrenia, or delusional disorder Increase in goal-directed activity or psychomotor agitation for at least 1 week Distractibility for at least 1 week

8B. Diagnosis of Psychotic Mania[Question 6]

The two most important diagnostic features for psychotic mania are hallucinations or delusions and elevated, expansive, or irritable mood. The experts endorsed the same additional features as for nonpsychotic mania, but placed more emphasis on ruling out schizophrenia, schizoaffective disorder, and delusional disorder as well the effects of drugs and other substances.

(***bold italics*** = features rated "extremely important" by at least 50% of the experts)

Most important discriminating features	Also consider
Hallucinations or delusions that occur only when the manic symptoms are also present ***Elevated, expansive, or irritable mood that persists for at least 1 week*** Inflated self-esteem or grandiosity for at least 1 week Flight of ideas or subjective experience that thoughts are racing, occurring frequently for at least 1 week Decreased need for sleep for at least 1 week The symptoms are not better accounted for by schizoaffective disorder, schizophrenia, or delusional disorder Excessive involvement in pleasurable activities that have a high potential for negative consequences (e.g., buying sprees, foolish business investments) No evidence that the patient has recently used a drug (e.g., cocaine, antidepressant medication) that can cause manic symptoms	Workup rules out a medical illness (e.g., multiple sclerosis, stroke) that could be causing the manic symptoms Increase in goal-directed activity or psychomotor agitation for at least 1 week Distractibility for at least 1 week

8C. Selecting Treatments for Mania[Question 26]

The first-line recommendation for ***mild mania*** was a mood stabilizer alone. The experts would also consider discontinuing an antidepressant if the patient is receiving one.

For ***severe nonpsychotic mania***, the experts would first discontinue any antidepressant the patient may be receiving and would treat the patient with a mood stabilizer combined with an antipsychotic. They would also consider using a mood stabilizer alone.

For ***psychotic mania***, the treatment of choice was a mood stabilizer combined with an antipsychotic (rated first line by 98% of the experts). The experts also recommended discontinuing any antidepressant the patient may be receiving. High second-line options for psychotic mania were ECT, a mood stabilizer plus an antipsychotic plus a benzodiazepine, or an antipsychotic alone. The editors note that one might consider using an antipsychotic alone if there is concern about delirium developing.

There was no first-line recommendation for treating a ***mixed episode***; high second-line options were a mood stabilizer plus an antipsychotic or a mood stabilizer alone.

(***bold italics*** = treatment of choice)

	Preferred	**Also consider**
Mild mania	A mood stabilizer alone	Discontinue antidepressant if patient is currently receiving one
Severe nonpsychotic mania**	Discontinue antidepressant if patient is currently receiving one* A mood stabilizer plus an antipsychotic*	A mood stabilizer alone**
Psychotic mania	***A mood stabilizer plus an antipsychotic*** Discontinue antidepressant if patient is currently receiving one*	Electroconvulsive therapy (ECT) A mood stabilizer plus an antipsychotic plus a benzodiazepine An antipsychotic alone
Mixed episode	*(None)*	A mood stabilizer plus an antipsychotic A mood stabilizer alone

*Very high second line.

**57% of the experts rated a mood stabilizer plus an antipsychotic first line (with 32% giving it a rating of "9") and 48% of the experts rated a mood stabilizer alone first line.

8D. Selecting Antipsychotics for Use in Combination With a Mood Stabilizer to Treat Mania With Psychosis[Question 27]

Risperidone and olanzapine at the dosages shown below were first-line options for use in combination with a mood stabilizer to treat mania with psychosis. Quetiapine was a high second-line choice. Although the experts gave high second-line ratings to a combination of a mood stabilizer and an antipsychotic in severe nonpsychotic mania, there was less support for the specific antipsychotics we asked about in nonpsychotic mania than in psychotic mania, with risperidone, olanzapine, and quetiapine all rated second line, probably reflecting less support for using an antipsychotic in nonpsychotic than psychotic mania. If it is decided to use an antipsychotic drug to treat nonpsychotic mania, the experts would recommend using slightly lower doses.

Preferred	**Also consider**
Risperidone 1.25–3.0 mg/day Olanzapine 5–15 mg/day	Quetiapine 50–250 mg/day

Note from the editors: We asked the experts about the diagnosis and treatment of a number of other conditions in elderly patients: panic disorder, generalized anxiety disorder, hypochondriasis, neuropathic pain, severe nausea and vomiting due to chemotherapy, motion sickness, irritability and hostility in the absence of a major psychiatric syndrome, and insomnia/sleep disturbance in the absence of a major psychiatric syndrome or discrete medical cause. Although the experts did not recommend the use of antipsychotics for any of these conditions, we present their recommendations concerning the diagnosis and treatment of these conditions in Guidelines 9–12 in an effort to make these guidelines as clinically useful as possible for all clinicians who treat elderly patients, including primary care physicians and internists.

Guideline 9: Panic Disorder

9A. Diagnosis of Panic Disorder[Question 7]

The features that the experts considered most important in diagnosing panic disorder in an older patient agree closely with the DSM-IV criteria. The experts considered recurrent unexpected panic attacks the most important discriminating feature.

(***bold italics*** = features rated "extremely important" by at least 50% of the experts)

Most important discriminating features	Also consider
Recurrent unexpected panic attacks (attacks that occur spontaneously "out of the blue") Persistent concern about having another panic attack or about the implications of the attack Significant change in daily behavior as a result of the panic attack No evidence that the patient has recently used drugs (e.g., psychostimulants) that can cause panic attacks or autonomic arousal Workup rules out a medical illness (e.g., hyperthyroidism) that could be causing the panic attack symptoms	*(None)*

9B. Selecting Treatments for Panic Disorder[Question 21]

The experts' first-line recommendation for treating panic disorder in an older patient was an antidepressant. High second-line options were CBT or the combination of an antidepressant plus a benzodiazepine. The experts did not recommend the use of an antipsychotic to treat panic disorder.

Preferred	Also consider
An antidepressant	Cognitive-behavioral therapy (CBT) An antidepressant plus a benzodiazepine

Guideline 10: Generalized Anxiety Disorder

10A. Diagnosis of Generalized Anxiety Disorder[Question 8]

The features that the experts considered most important in diagnosing generalized anxiety disorder in an older patient agree closely with the DSM-IV criteria. The experts considered excessive anxiety and worry that occur more days than not for at least 6 months the most important discriminating feature.

(***bold italics*** = features rated "extremely important" by at least 50% of the experts)

Most important discriminating features	Also consider
Excessive anxiety and worry that occur more days than not for at least 6 months The person finds it hard to control the anxiety and worry The worry is accompanied by a feeling of restlessness or being keyed up	No evidence that the patient has recently used drugs (e.g., excessive caffeine intake) that can cause anxiety Workup rules out a medical illness (e.g., hyperthyroidism) that could be causing the anxiety The person has difficulty concentrating (mind going blank) Presence of muscle tension Sleep disturbance (difficulty falling or staying asleep, restless unsatisfying sleep) The person becomes easily fatigued

10B. Selecting Treatments for Generalized Anxiety Disorder[Question 22]

The experts recommended an antidepressant for the treatment of generalized anxiety disorder (a very high second-line option rated first line by 67% of the experts). Other high second-line options were a benzodiazepine, CBT, or the combination of an antidepressant and a benzodiazepine. The experts did not recommend the use of an antipsychotic to treat generalized anxiety disorder.

Preferred	Also consider
An antidepressant*	A benzodiazepine Cognitive-behavioral therapy (CBT) An antidepressant plus a benzodiazepine

*Very high second line.

Guideline 11: Hypochondriasis

11A. Diagnosis of Hypochondriasis[Question 9]

The features that the experts considered most important in diagnosing hypochondriasis in an older patient agree closely with the DSM-IV criteria. The experts considered persistent fears of having a serious disease that persist despite appropriate medical evaluation and reassurance the most important discriminating feature. The presence of multiple medically confirmed problems was not considered important in ruling out the diagnosis.

(***bold italics*** = features rated "extremely important" by at least 50% of the experts)

Most important discriminating features	Also consider
Persistent fears of having a serious disease based on a misinterpretation of bodily symptoms ***The preoccupation persists despite appropriate medical evaluation and reassurance*** Although the person may not recognize that the concern is excessive, the belief is not of delusional intensity (as in delusional disorder)	*(None)*

11B. Selecting Treatments for Hypochondriasis[Question 23]

There was no first-line consensus among the experts on the most appropriate treatment for hypochondriasis. High second-line options they would consider are supportive therapy, CBT, or an antidepressant. The experts did not recommend the use of an antipsychotic to treat hypochondriasis.

Preferred	Also consider
(None)	Supportive therapy CBT An antidepressant

Guideline 12: Selecting Treatments for Other Indications[Questions 28–36]

The experts did not recommend the use of an antipsychotic agent for any of the conditions listed below. If a patient with ***neuropathic pain*** has failed to respond to or tolerate a nonsteroidal anti-inflammatory agent and/or a cyclo-oxygenase-2 inhibitor, the experts considered an anticonvulsant the first-line treatment option, with a tricyclic antidepressant a high second-line alternative. For ***severe nausea and vomiting due to chemotherapy***, a 5-HT_3 antagonist (e.g., odansetron or granisetron) was rated high second line. For ***motion sickness***, the expert preferred an antihistamine such as Dramamine or meclizine and would also consider an anticholinergic agent such as scopolamine. For ***irritability/hostility in the absence of a major psychiatric syndrome*** (dementia, depression, mania, schizophrenia), psychotherapy was rated high second line, followed by treatment with an SSRI, with little support for any other medication treatments. For ***insomnia/sleep disturbance in the absence of a major psychiatric syndrome or discrete medical cause*** (e.g., sleep apnea, congestive heart failure with nocturnal dyspnea), high second-line options were a hypnotic agent, such as zolpidem or zaleplon, or a sedating antidepressant such as trazodone or mirtazapine.

	Preferred	**Also consider**
Neuropathic pain*	An anticonvulsant (e.g., carbamazepine, gabapentin)	A tricyclic antidepressant
Severe nausea and vomiting due to chemotherapy	*(None)*	A 5-HT_3 antagonist (e.g., odansetron [Zofran], granisetron [Kytril])
Motion sickness	An antihistamine (e.g., Dramamine, meclizine [Antivert, Bonine])**	An anticholinergic agent (e.g., scopolamine, Transderm scopolamine patch)
Irritability and hostility in the absence of a major psychiatric syndrome	*(None)*	Psychotherapy An SSRI
Insomnia/sleep disturbance in the absence of a major psychiatric syndrome or a discrete medical cause	*(None)*	Other hypnotic agent (e.g., zolpidem, zaleplon, chloral hydrate) A sedating antidepressant (e.g., trazodone, mirtazapine)

*Assume that the patient has failed to respond to or been unable to tolerate treatment with a nonsteroidal anti-inflammatory drug (NSAID) (e.g., ibuprofen) and/or a cyclo-oxygenase-2 (COX-2) inhibitor (e.g., celecoxib [Celebrex]).

**Very high second line.

III. Duration of Treatment

Guideline 13: Frequency of Follow-Up Monitoring for Patients on Antipsychotics[Question 37]

The table below summarizes the experts' recommendations concerning optimal and longest acceptable follow-up intervals when monitoring elderly patients who are receiving antipsychotics. Note that the intervals listed in the table are based on the median of the respondents' write-in answers (see Survey Question 37). The editors note that there was a high level of agreement between the psychiatrists and the geriatric internists/family physicians who completed this question.

Clinical situation	**Optimal follow-up interval**	**Longest acceptable follow-up interval**
After starting an antipsychotic	1 week	2 weeks
After a change in the dose of the antipsychotic	10 days	4 weeks
Once a patient has been symptomatically stable on the same dose of antipsychotic for 1 month, to monitor for continued therapeutic benefit and tolerability	2 months	3 months
Once a patient is in maintenance treatment (i.e., has been stable on the same antipsychotic medication for at least 6 months), to monitor for continued therapeutic benefit and tolerability	3 months	6 months

Guideline 14: Duration of Antipsychotic Treatment[Questions 38 & 39]

The table below summarizes the experts' recommendations concerning 1) how long they would continue antipsychotic treatment before changing the dose or switching to a different medication if the patient is having an inadequate response and 2) how long they would continue treatment with an antipsychotic after response before trying to discontinue the medication. Note that the intervals listed in the table are based on the median of the respondents' write-in answers (see Survey Questions 38 and 39). The editors note that again there was a high level of agreement between the psychiatrists and the internists/primary care physicians who completed the survey on this question.

Disorder	**Duration of treatment before changing dose or medication if response inadequate**	**Duration of treatment after response before trying to discontinue**
Delirium*	1 day	1 week
Dementia with agitation and delusions**	5 days	3 months
Dementia with agitation without delusions**	7 days	3 months
Schizophrenia***	2 weeks	Indefinitely
Delusional disorder***	2 weeks	6 months–indefinitely
Agitated nonpsychotic major depression	1 week	2 months
Psychotic major depression	1 week	6 months
Nonpsychotic major depression with severe anxiety****	2 weeks	2 months
Mania with psychosis	5 days	3 months
Mania without psychosis	1 week	2 months

*Delirium is a medical emergency in which the demands of acute management require frequent reassessment of treatment response and rapid dosage adjustment. Note that many of the experts gave their response in terms of hours.

**If an older patient with dementia with agitation has responded well to treatment with an antipsychotic, the experts recommend waiting 3–6 months before trying to taper the dose to determine the lowest effective maintenance dose to prevent relapse.[Question 41]

***If an older patient with schizophrenia or delusional disorder has responded well to treatment with an antipsychotic, the experts recommend tapering to the lowest effective dose and then continuing treatment indefinitely.[Question 40] When asked to write in how long they would continue treatment after response in delusional disorder, 31% said they would continue indefinitely; the median of all responses was 6 months.

****Approximately a third of the experts indicated that they would not generally use an antipsychotic to treat nonpsychotic major depression with severe anxiety.

IV. Complicating Conditions That Influence Treatment Selection and Dosing

Guideline 15: Selecting Antipsychotics for a Patient With a Complicating Condition[Questions 42 & 43]

The experts would avoid clozapine, olanzapine, and conventional antipsychotics, especially low and mid-potency agents, in patients who have diabetes, obesity, or dyslipidemia. They would avoid clozapine, ziprasidone, and conventional antipsychotics, especially low- and mid-potency agents, in patients with QTc prolongation or congestive heart failure. They preferred quetiapine or olanzapine for patients with prolactin-related disorders such as galactorrhea or gynecomastia and quetiapine for patients with Parkinson's disease. The experts preferred risperidone, with quetiapine high second line, for patients with cognitive impairment, constipation, diabetes mellitus, diabetic neuropathy, dyslipidemia, xerophthalmia, and xerostomia.

	If low dose indicated		**If medium/high dose indicated**	
Complicating condition	**Preferred**	**Also consider**	**Preferred**	**Also consider**
Cognitive impairment	Risperidone	Quetiapine Olanzapine	Risperidone	Quetiapine
QTc prolongation	*(None)*	Risperidone Olanzapine Quetiapine	*(None)*	Risperidone Quetiapine Olanzapine
Congestive heart failure	*(None)*	Risperidone Quetiapine Olanzapine Aripiprazole	*(None)*	Quetiapine Risperidone Olanzapine
Constipation	Risperidone	Quetiapine Olanzapine	*(None)*	Risperidone Quetiapine
Dysphagia	*(None)*	Risperidone Quetiapine Olanzapine	*(None)*	Quetiapine Risperidone Olanzapine
Diabetes mellitus	Risperidone	Quetiapine Aripiprazole	*(Same as low dose)*	
Diabetic neuropathy	Risperidone	Quetiapine	*(Same as low dose)*	
Dyslipidemia	Risperidone	Quetiapine	*(Same as low dose)*	
Failure to thrive	*(None)*	Olanzapine Quetiapine Risperidone	*(None)*	Risperidone Quetiapine Olanzapine
Gait disturbance/ history of falls	*(None)*	Quetiapine Risperidone	*(Same as low dose)*	
Galactorrhea	*(None)*	Quetiapine Olanzapine	*(Same as low dose)*	
Gynecomastia	*(None)*	Quetiapine Olanzapine	*(Same as low dose)*	
Disorders of excessive daytime somnolence (e.g., narcolepsy)	*(None)*	Risperidone	*(Same as low dose)*	

Guideline 15: continued

Complicating condition	If low dose indicated		If medium/high dose indicated	
	Preferred	**Also consider**	**Preferred**	**Also consider**
Narrow angle glaucoma	*(None)*	Risperidone Quetiapine	*(Same as low dose)*	
Obesity	*(None)*	Risperidone	*(None)*	Risperidone Quetiapine
Orthostatic hypotension	*(None)*	Risperidone	*(None)*	Risperidone Quetiapine
Osteoporosis	*(None)*	Quetiapine Risperidone Olanzapine	*(None)*	Quetiapine Olanzapine Risperidone
Parkinson's disease	Quetiapine	Olanzapine Clozapine	Quetiapine	*(None)*
Retinopathy (e.g., macular degeneration)	*(None)*	Risperidone Olanzapine Quetiapine	*(None)*	Risperidone Olanzapine
Sleep apnea	*(None)*	Risperidone Quetiapine	*(Same as low dose)*	
Urinary retention (prostatism)	*(None)*	Risperidone Quetiapine	*(Same as low dose)*	
Xerophthalmia	Risperidone	Quetiapine	*(None)*	Risperidone Quetiapine
Xerostomia	Risperidone	Quetiapine	*(None)*	Risperidone Quetiapine

V. Drug-Drug Interactions and Side Effects

Guideline 16: Combining Medications in Older Patients[Question 44]

The experts recommended close monitoring for side effects when using the combinations listed in the table below. More than a quarter of the experts considered the following combinations to be contraindicated: clozapine + carbamazepine (rated as contraindicated by 39% of the experts), ziprasidone + a tricyclic antidepressant (TCA) (rated as contraindicated by 26%), and a low-potency conventional antipsychotic + fluoxetine (rated as contraindicated by 27%). Certain combinations of medications caused the experts more concern (e.g., drugs that are potent inhibitors of CYP drug-metabolizing enzymes and thus have increased potential to cause drug-drug interactions). These issues are discussed in more detail in the introduction to these guidelines.

Extra monitoring for side effects needed when combining an antipsychotic with:			
	An antidepressant	**A mood stabilizer**	**Other drugs**
Aripiprazole	Paroxetine, nefazodone, TCA, MAOI	Lithium, carbamazepine, lamotrigine	Codeine, ketoconazole, phenytoin
Clozapine	Fluoxetine, fluvoxamine, paroxetine, sertraline, bupropion, mirtazapine, nefazodone, trazodone, TCA, MAOI	Lithium, **carbamazepine,*** gabapentin, lamotrigine, valproate	Atenolol, caffeine, captopril, codeine, corticosteroids, digoxin, ketoconazole, loratadine, macrolide antibiotics, nifedipine, phenytoin, theophylline, tramadol, warfarin
Olanzapine	Fluoxetine, fluvoxamine, paroxetine, mirtazapine, nefazodone, TCA, MAOI	Lithium, carbamazepine, lamotrigine, valproate	Codeine, phenytoin, theophylline, tramadol
Quetiapine	Fluvoxamine, nefazodone, TCA, MAOI	Lithium, carbamazepine, lamotrigine, valproate	Codeine, ketoconazole, loratadine, phenytoin, tramadol
Risperidone	Fluoxetine, paroxetine, nefazodone, TCA, MAOI	Lithium, carbamazepine, lamotrigine	Codeine, phenytoin, tramadol
Ziprasidone	Fluoxetine, fluvoxamine, paroxetine, nefazodone, **TCA,*** MAOI	Lithium, carbamazepine, lamotrigine, valproate	Codeine, digoxin, ketoconazole, phenytoin, tramadol
High-potency conventional	Fluoxetine, fluvoxamine, paroxetine, TCA, MAOI	Lithium, carbamazepine, lamotrigine	Codeine, phenytoin, tramadol
Mid-potency conventional	Fluoxetine, fluvoxamine, paroxetine, nefazodone, TCA, MAOI	Lithium, carbamazepine, lamotrigine, valproate	Atenolol, captopril, digoxin, codeine, loratadine, nifedipine, phenytoin, tramadol
Low-potency conventional	**Fluoxetine,*** fluvoxamine, paroxetine, mirtazapine, trazodone, nefazodone, TCA, MAOI	Lithium, carbamazepine, gabapentin, lamotrigine, valproate	Atenolol, captopril, codeine, digoxin, loratadine, macrolide antibiotics, nifedipine, phenytoin, tramadol

*These three combinations (clozapine + carbamazepine, ziprasidone + a TCA, and a low-potency conventional antipsychotic + fluoxetine) were rated as contraindicated by more than 25% of the experts. The editors note that these combinations should probably be avoided if possible or used very cautiously.

Guideline 17: Selecting Antipsychotics for a Patient With a History of Side Effects[Questions 45 & 46]

The experts preferred quetiapine for patients with extrapyramidal side effects (EPS), tardive dyskinesia (TD), or hyperprolacinemia. They preferred risperidone for patients with excessive daytime sedation. The experts would avoid conventional antipsychotics and clozapine in patients with a history of central anticholinergic syndrome or significant peripheral anticholinergic syndrome, tachycardia, or drug-induced orthostatic hypotension. They would avoid conventional antipsychotics in patients with a history of EPS, TD, or hyperprolactinemia. They would avoid clozapine and mid- or low-potency conventional antipsychotics in a patient with a history of excessive daytime sedation.

	If low dose indicated		**If medium/high dose indicated**	
Patient has a history of	**Preferred**	**Also consider**	**Preferred**	**Also consider**
Central anticholinergic syndrome	*(None)*	Risperidone Quetiapine Aripiprazole		Risperidone Quetiapine Aripiprazole
Significant peripheral anticholinergic side effects		Risperidone Quetiapine Aripiprazole		Risperidone Quetiapine Aripiprazole
Drug-induced orthostatic hypotension		Aripiprazole Risperidone Quetiapine		Risperidone Quetiapine
Excessive daytime sedation	Risperidone	Aripiprazole		Risperidone
Extrapyramidal side effects (drug-induced reversible motor side effects)	Quetiapine	Olanzapine Aripiprazole	Quetiapine	Aripiprazole Olanzapine
Hyperprolactinemia		Quetiapine Aripiprazole Olanzapine		Quetiapine Olanzapine
Tachycardia		Risperidone Quetiapine Olanzapine		Risperidone Quetiapine Aripiprazole
Tardive dyskinesia*	Quetiapine	Olanzapine Aripiprazole Clozapine		Quetiapine Olanzapine

*If an older patient develops a dyskinesia while receiving an antipsychotic, but the clinician believes the patient's condition requires continued treatment with a psychotropic medication, the experts recommend continuing treatment with an antipsychotic medication, but switching to an alternate agent that has a lower liability for causing TD if possible. They would also consider tapering the current antipsychotic to the lowest possible dose.[Question 47]