The Expert Consensus Guideline Series

Treatment of Agitation in Older Persons with Dementia

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The following participants in the Expert Consensus Survey were identified from several sources: recent research publications and funded grants, the DSM-IV advisers for dementia, delirium, and other cognitive disorders, the Task Force for the American Psychiatric Association's *Practice Guidelines for the Treatment of Patients with Alzheimer's Disease and Other Disorders of Late Life*, and those who have worked on other dementia guidelines. Of the 100 experts to whom we sent the geriatric agitation survey, 84 (84%) replied. The recommendations in the guidelines reflect the aggregate opinions of the experts and do not necessarily reflect the opinion of each individual on each question.

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One additional panel member wished to remain anonymous.

Contents

Preface

The McGraw-Hill Healthcare Information Programs Division is pleased to publish the newest title in The Expert Consensus Guidelines Series, *Treatment of Agitation in Older Persons with Dementia*. The development of the practice guidelines described in this publication have employed the latest survey techniques and reflect only the most current clinical standards. The result is a practical reference tool not only for clinicians, but also for administrators, mental health educators, and other healthcare professionals involved in the care of patients who have dementia. These guidelines, assembled under the expert direction of the steering committee composed of Docherty, Frances, and Kahn, are designed to be easy to follow and to use.

Treating the agitated dementia patient is, of course, never easy. Episodes of agitation add to what is most likely an already stressed family situation. In addition, the array of pharmacologic interventions can be difficult to understand and deploy, especially by physicians who work in primary care practice settings where they see only an occasional dementia patient.

These guidelines offer a "one stop" reference. The guidelines take readers through the initial diagnosis of agitation and offer guidance for the overall and long-term management—from environmental interventions to suggested medications for several common scenarios. The specific syndromes of agitation, including delirium, psychosis, depression, anxiety, insomnia, "sundowning," aggression and anger, and pain, are outlined in detail. Initial and secondary options are presented for each syndrome, along with advice regarding multiple vs. single drug therapy, side effects, and inadequate response to therapy. The section *A Guide for Families and Caregivers* (p. 81) is exceptionally well done and will be practical for use by both groups.

I have already used the draft copy of the guidelines several times in my own practice. The printed publication now will become a member of my reference library, no doubt proving to be a valuable addition as my patient population continues to age. I hope you find the guidelines to be as beneficial.

William O. Roberts, M.D.

Editor-in-Chief
McGraw-Hill Healthcare
Information Programs

Introduction

How often have you wished that you had an expert on hand to advise you on how best to help a patient who is not responding well to treatment or is having a serious complication? Unfortunately, of course, an expert is usually not at hand, and even if a consultation were available, how would you know that any one expert opinion represents the best judgment of our entire field? This is precisely why we began the Expert Consensus Guidelines Series. Our practical clinical guidelines for treating the major mental disorders are based on a wide survey of the best expert opinion and are meant to be of immediate help to you in your everyday clinical work. Let's begin by asking and answering four questions that will help put our effort in context.

How do these Expert Consensus Guidelines relate to (and differ from) the other guidelines for dementia and Alzheimer's disease that are already available in the literature?

These guidelines build upon existing guidelines (as have our previous guidelines*) but go beyond them in a number of ways:

1. We have focused exclusively on the problem of agitation rather than on broader issues such as the evaluation and treatment of cognitive deficits.
2. We focus our questions on the most specific and crucial treatment decisions for which detailed recommendations are usually not made in the more generic guidelines that are currently available.
3. We survey the opinions of a very large number (65–100) of the leading experts in each field and have achieved a remarkably high rate of survey response (at least 84% for each of the disorders), ensuring that our recommendations are authoritative and represent the best in current expert opinion.
4. We report the experts' responses to each question in a detailed and quantified way (but one that is easy to understand) so that you can evaluate the relative strength of expert opinion supporting the guideline recommendations.
5. The guidelines are presented in a simple and well-organized format that makes it easy to find exactly where each patient's problem fits in and what the experts would suggest you do next.

Why should we base current treatment decisions on expert consensus instead of the relevant treatment studies in the research literature?

There are three reasons why expert consensus remains important:

1. Most research studies are difficult to generalize to clinical practice because they make internal validity the highest priority and require rigorous patient selection criteria and experimental controls. We need practice guidelines for help with precisely those patients who would not meet the narrow selection criteria used in most research studies. The typical patient who causes us the most concern in clinical practice usually presents with comorbid disorders and/or has not responded to previous treatment efforts and/or requires a number of different treatments delivered in combination or sequentially. Such individuals are almost universally excluded from clinical trials.

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*Kahn DA, Carpenter D, Docherty JP, Frances A. The expert consensus guideline series: Treatment of bipolar disorder. J Clin Psychiatry 1996;57(Suppl 12A)

McEvoy JP, Weiden PJ, Smith TE, Carpenter D, Kahn DA, Frances A. The expert consensus guideline series: Treatment of schizophrenia. J Clin Psychiatry 1996;57(Suppl 12B)

March JS, Frances A, Carpenter D, Kahn DA. The expert consensus guideline series: Treatment of obsessive-compulsive disorder. J Clin Psychiatry 1997;58(Suppl 4)

2. The available controlled research studies do not, and cannot possibly, address all the variations and contingencies that arise in clinical practice. Expert-generated guidelines are needed because clinical practice is so complicated that it is constantly generating far too many questions for the clinical research literature to ever answer comprehensively with systematic studies.
3. Changes in the accepted best clinical practice often occur at a much faster rate than the necessarily slower paced research efforts that would provide scientific documentation for the change. As new treatments become available, clinicians often find them to be superior for many indications that go far beyond narrower indications supported by the available controlled research.

For all these reasons, the aggregation of expert opinion is a crucial bridge between the clinical research literature and clinical practice in developing practice guidelines.

How valid are the expert opinions provided in these guidelines and how much can I trust the recommendations?

The honest answer for many of the questions is that we simply don't know. Expert opinion must always be subject to the corrections provided by the advance of science. Moreover, precisely because we asked the experts about the most difficult questions facing you in clinical practice, many of their recommendations must inevitably be based on incomplete research information and may have to be revised as we learn more. Despite this, the aggregation of the universe of expert opinion is often the best tool we have to develop guideline recommendations. Certainly the quantification of the opinions of a large number of experts is likely to be much more trustworthy than the opinions of any small group of experts or of any single person.

Why do I have to use treatment guidelines?

First, no matter how skillful or artful any of us may be, there are frequent occasions when we feel the need for expert guidance and external validation of our clinical experience. Moreover, our field is becoming standardized at an ever more rapid pace. The only question is, who will be setting the standards? We believe that practice guidelines should be based on the very best in clinical and research opinion. Otherwise, they will be dominated by other less clinical and less scientific goals (e.g., pure cost reduction, bureaucratic simplicity). It should be of some comfort to those who are concerned about losing their clinical art under the avalanche of guidelines that the complex specificity of clinical practice will always require close attention to the individual clinical situation. Guidelines provide useful information but are never a substitute for good clinical judgment and common sense.

We hope that our guidelines will be widely used and will be useful not only to clinicians and case managers but also to policy makers, administrators, mental health educators, patient advocates, and clinical and health services researchers. Ultimately, of course, the purpose of this whole enterprise is to do whatever we can to improve the lives of our patients. It is our hope that the expert advice provided in these guidelines will make our treatments ever more specific and effective.

John P. Docherty, M.D.
Allen Frances, M.D.
David A. Kahn, M.D.

How to Use the Guidelines

ORGANIZATION OF THE GUIDELINES

The guidelines are organized so that clinicians can locate their patients at any phase of illness and quickly find the experts' treatment recommendations. At the beginning, we provide two **executive summaries** of the recommendations that can be kept at your desk as a quick reference. The first summary is organized according to clinical situations (p. 12) and the second according to the indications for specific somatic treatments (p. 13) Next, we present **treatment selection algorithms** that summarize some of the same treatment information in visual format (p. 14).

The treatment recommendations are then given in nine individual **guidelines** that present the strategies in an easy-to-use tabular format.

Guideline 1: Assessment of Agitation in Dementia

Guideline 2: Overall Management Strategies

Guideline 3: Selecting Environmental Interventions

Guideline 4: Selecting Medications for Specific Syndromes of Agitation

Guideline 5: Managing Inadequate Response to Medication

Guideline 6: Long-Term Treatment Issues

Guideline 7: Selecting Specific Medications within Different Classes of Drugs

Guideline 8: Dose and Side Effects

Guideline 9: Safety and Tolerability

The guidelines are followed by an **appendix** that contains the Mini-Mental State Examination (p. 38) and a list of **suggested readings** (p. 39).

The data supporting the recommendations given in the guidelines are referenced by means of numbered notes on the guideline pages. These notes refer to specific questions and answers in the expert survey that were used to develop the guideline recommendations. The actual questions and results of the expert survey are presented in their entirety in the second half of this publication (pp. 43–80).

Finally, we include an educational **guide for families and caregivers** (p. 81) that can be reproduced for distribution to families and caregivers. We gratefully acknowledge the American Federation for Aging Research, the American Association for Retired Persons, and the National Citizens' Coalition for Nursing Home Reform for working with us to develop these educational materials.

We begin at the point of treatment, assuming familiarity with assessment and diagnostic issues as presented in DSM-IV* and other standard sources. We also encourage a thorough reading of available professional and lay press publications on the diagnosis and treatment of agitation in dementia that are listed in the *Suggested Readings* section of this guideline (p. 39). Because our questionnaires could not cover every possible topic of interest, there are a few occasions when we added our own recommendations based on our reading of the available literature. You can easily identify the expert consensus recommendations because they are always footnoted. Our own editorial additions are also clearly noted as such.

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*American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Washington, DC: American Psychiatric Association; 1994

METHODS

The Survey

The editors of the guidelines first created a skeleton algorithm based on the standard literature to identify key decision points in the everyday treatment of patients with agitation due to dementia. We highlighted points where the literature was indefinite and then developed a written questionnaire concerning these treatment issues. The questionnaire used a 9-point scale slightly modified from a survey format developed by the RAND Corporation for ascertaining expert consensus.* The experts were told not to consider costs when making their ratings. We presented the rating scale to the experts with the following instructions:

1 2 3 4 5 6 7 8 9

You should use scores in the range of 7–9 to indicate the degree of appropriateness, 4–6 the degree of equivocal opinion, and 1–3 the degree of inappropriateness, with the following anchor points:

- 1 = extremely inappropriate—a treatment you would never use
- 2–3 = usually inappropriate—a treatment you would rarely use
- 4–6 = equivocal—a second line treatment you would sometimes use (e.g., if first line inappropriate or ineffective)
- 7–8 = appropriate—a first-line treatment you would often use
- 9 = extremely appropriate—this is your treatment of choice (may have more than one per question)

We asked questions to determine the experts' opinions about 33 clinical situations. The questionnaire was sent to 100 leading experts on agitation in dementia, who were identified from the following sources: recent research publications and funded grants, the DSM-IV advisers for dementia, delirium, and other cognitive disorders, the Task Force for the American Psychiatric Association's *Practice Guidelines for the Treatment of Patients with Alzheimer's Disease and Other Disorders of Late Life*, and those who have worked on other dementia guidelines. Of the 100 experts, 84 (84%) responded to the survey. Here is an example of our question format:

6. Please rate each of the following for a patient with severe agitation dominated by prominent psychotic symptoms, including actions resulting from delusions or hallucinations. Please rate each item separately for both short-term/p.r.n. and long-term use.

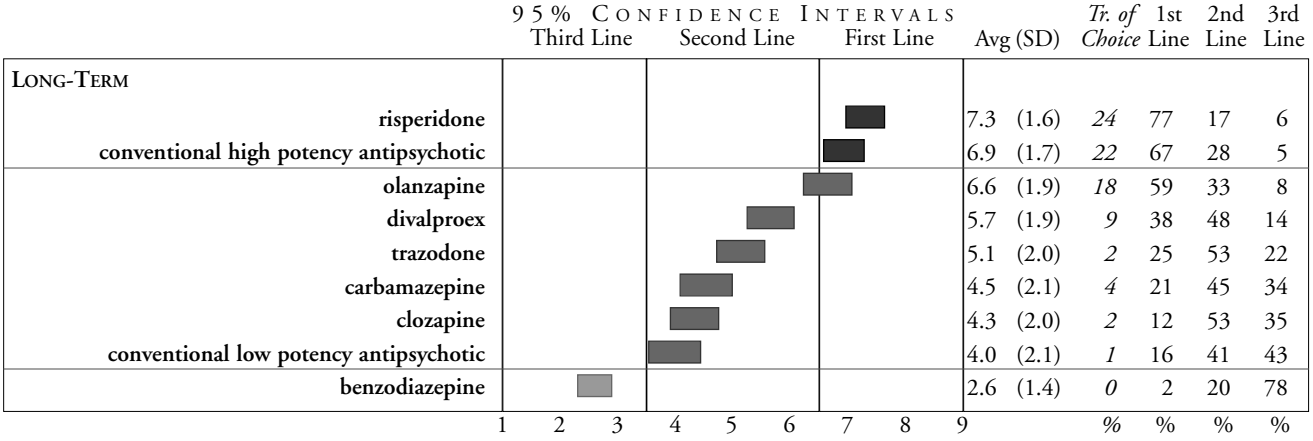
LONG-TERM:	a) benzodiazepine	1 2 3	4 5 6	7 8 9
	b) carbamazepine	1 2 3	4 5 6	7 8 9
	c) clozapine	1 2 3	4 5 6	7 8 9
	d) conventional high potency antipsychotic	1 2 3	4 5 6	7 8 9
	e) conventional low potency antipsychotic	1 2 3	4 5 6	7 8 9
	f) divalproex	1 2 3	4 5 6	7 8 9
	g) olanzapine	1 2 3	4 5 6	7 8 9
	h) risperidone	1 2 3	4 5 6	7 8 9
	i) trazodone	1 2 3	4 5 6	7 8 9

*Brook RH, Chassin MR, Fink A, et al. A method for the detailed assessment of the appropriateness of medical technologies. International Journal of Technology Assessment in Health Care 1986;2:53–63

The results of Survey Question 6 for long-term treatment options are presented graphically as shown below, with the confidence intervals for each treatment option shown as horizontal bars and the numerical values given in the table on the right. In analyzing the results of the survey questions, we first calculated the mean (Avg), standard deviation (SD), and confidence interval (CI) for each item. The CI is a statistically calculated range which tells you that, if the survey were repeated with a similar group of experts, there is a 95% chance that the mean score would fall within that range. We designated a rating of first, second, or third line for each item on which there was consensus. This rating was determined by the category into which the 95% CI of its mean score fell.

6 Please rate each of the following for a patient with severe agitation dominated by prominent PSYCHOTIC SYMPTOMS, including actions resulting from delusions or hallucinations. Please rate each item separately for both short-term/p.r.n. and long-term use.

Comment: For longer-term management of psychotic symptoms accompanying dementia and agitation, the experts recommend risperidone followed by a conventional antipsychotic as first line options. Olanzapine is a highly rated second line option. Atypical antipsychotics have a lower risk than conventional antipsychotics of causing extrapyramidal symptoms in long-term treatment of most patients with dementia. Divalproex and trazodone are options to consider if an antipsychotic is not effective. It should be noted that this expert survey was done before quetiapine and other newer atypical antipsychotics were available.



	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
LONG-TERM					
risperidone	7.3 (1.6)	*24*	77	17	6
conventional high potency antipsychotic	6.9 (1.7)	*22*	67	28	5
olanzapine	6.6 (1.9)	*18*	59	33	8
divalproex	5.7 (1.9)	*9*	38	48	14
trazodone	5.1 (2.0)	*2*	25	53	22
carbamazepine	4.5 (2.1)	*4*	21	45	34
clozapine	4.3 (2.0)	*2*	12	53	35
conventional low potency antipsychotic	4.0 (2.1)	*1*	16	41	43
benzodiazepine	2.6 (1.4)	*0*	2	20	78
		%	%	%	%

THE RATINGS

The following types of ratings appear in the survey results:

First line treatments are those strategies that the expert panel feels are usually appropriate as initial treatment for a given situation. Treatment of choice, when it appears, is an especially strong first line recommendation (having been rated as "9" by at least half the experts). Treatments of choice are indicated with a star in the survey results graphic. In choosing between several first line recommendations, or deciding whether to use a first line treatment at all, clinicians should consider the overall clinical situation, including the patient's prior response to treatment, side effects, general medical problems, and patient preferences.

Second line treatments are reasonable choices for patients who cannot tolerate or do not respond to the first line choices. Alternatively, you might select a second line choice as your initial treatment if the first line options are deemed unsuitable for a particular patient (e.g., because of poor previous response, inconvenient dosing regimen, particularly annoying side effects, a general medical contraindication, a potential drug interaction, or if the experts don't agree on a first line treatment).

For some questions, second line ratings dominated, especially when the experts did not reach any consensus on first line options. In such cases, to differentiate within the pack, we label those items whose confidence intervals overlap with the first line category as "top-tier second line."

Third line treatments are usually inappropriate or used only when preferred alternatives have not been effective.

No Consensus. For each item in the survey, we used a chi-square test to determine whether the experts' responses were randomly distributed across the three categories, which suggests a lack of consensus. These items are indicated by unshaded bars in the survey results.

Presentation of the Results

The survey results are presented graphically on pp. 44–80. For a detailed discussion of how to read the survey results, see p. 43.

HOW TO USE THE GUIDELINES

After the survey results were analyzed and ratings assigned, the next step was to turn these recommendations into user-friendly guidelines. For example, the results of Survey Question 6 presented above are shown on p. 51 and are used in *Guideline 4B: Selecting Medications for Specific Syndromes of Agitation: Psychosis* (p. 22). The experts rated risperidone, followed by a conventional high potency antipsychotic, as first line medications, with olanzapine, divalproex, and trazodone highly rated second line alternatives. Whenever the guideline gives more than one treatment in a rating category, we list them in the order of their mean scores.

Let's examine how a clinician might use the guidelines in selecting a treatment for a hypothetical patient with Alzheimer's disease living at home with a caregiver, who has been brought to the office because of the recent onset of mild agitation with psychosis. In the table of contents, the clinician would locate *Guideline 1: Assessment of Agitation in Dementia*, and go through a brief differential diagnosis, section 1A, focusing first on general medical conditions (as suggested in section 1B) and then on environmental and psychosocial factors. If medical problems were stable, the clinician would then turn to *Guideline 2*, and begin acute management with both environmental interventions (as outlined in *Guideline 3*) and probably medication. To select medication, the clinician would use the table of contents to locate the main clinical features of the agitation, in this case psychosis, and turn to *Guideline 4B*. For acute treatment, the clinician would then either select a conventional high potency antipsychotic (first line) or consider an atypical antipsychotic, based on side effect concerns and desired route of administration. Should the patient need long-term medication, risperidone or a conventional high potency antipsychotic would be chosen. If the patient did not respond to the initial treatment choice, the clinician could consult *Guideline 5* to learn that the environment should be re-evaluated, and that the medication should be switched to (not combined with) a suggested next choice. Once the patient has improved, *Guideline 6* suggests how long the specific medication should be continued before tapering. The remaining guidelines provide details on dosing, drug interactions, emergent side effects, and safety issues.

LIMITATIONS AND ADVANTAGES OF THE GUIDELINES

These guidelines can be viewed as an expert consultation, to be weighed in conjunction with other information and in the context of each individual patient-physician relationship. They do not replace clinical judgment. We describe groups of patients, and make suggestions intended to apply to the average patient in each group. **However, patients will differ greatly in their treatment preferences and capacities, in their history of response to previous treatments, their family history of treatment response, and their tolerance for different side effects. Therefore, the experts' preferred recommendations may not be appropriate in all circumstances.**

We remind readers of several other limitations of these guidelines:

1. The guidelines are based on a synthesis of the opinions of a large group of experts. From question to question, some individual experts may differ with the consensus view.
2. Precisely because we are asking crucial questions that are not yet well answered by the literature, we have relied on expert opinion. One thing that the history of medicine teaches us is that expert opinion at any given time can be very wrong. Accumulating research will ultimately reveal better and clearer answers. Clinicians should therefore stay abreast of the literature for developments that would make our recommendations obsolete. We also plan to revise the guidelines periodically based both on new research information and reassessment of expert opinion.
3. These guidelines are comprehensive but not exhaustive; because of the nature of our method, we omit some interesting topics on which we did not query the expert panel.

Despite these limitations, these guidelines represent a significant advance because of their specificity and the use of a large expert sample.

SUGGESTED TOUR

The best way to use these guidelines is first to read the *Table of Contents*, *Executive Summaries*, and *Treatment Algorithms* to get an overview of how the document is organized. Next, read through the individual guidelines. Finally, we find it fascinating to compare our own opinions with those of the experts on each of the questions; we strongly recommend that you use the detailed survey results presented in the second half of this publication in this way.

No set of guidelines can ever improve practice if read just once. These guidelines are meant to be used in an ongoing way, since each patient's status and phase of illness will require different interventions at different times. Locate your patient's problem or your question about treatment in the *Table of Contents*, and compare your plan with the guideline recommendations. We believe the guideline recommendations will reinforce your best judgment when you are in familiar territory, and help you with new suggestions when you are in a quandary. A **clinician feedback form** is included on the inside back cover. We hope that you will complete it and return it to us.

Agitation Executive Summary A:

Preferred Treatments by Clinical Situation

(***bold italic*** = first line)

CHAP = conventional high potency antipsychotic
SSRI = selective serotonin reuptake inhibitor

Overall Management

- Mild agitation → ***environmental intervention + medication***; consider environmental intervention alone
- Severe agitation → ***medication + environmental intervention***; consider medication alone

Choice of Environmental Intervention

- Both mild and severe agitation → ***education and support for family and caregivers***
- Mild agitation → ***structured routines, reassurance, socialization***
- Severe agitation → ***supervision and environmental safety***

Selecting Medications for Specific Presentations of Agitation

- Delirium (other than medication toxicity) → ***CHAP***
- Psychosis
  - long-term → ***risperidone; CHAP***
  - acute → ***CHAP***
- Depression
  - without psychosis → ***antidepressant alone: sertraline or paroxetine***
  - with psychosis → ***antidepressant + antipsychotic;*** or ***electroconvulsive therapy***
- Anxiety
  - long-term → buspirone
  - acute → benzodiazepine (lorazepam; consider oxazepam)
- Insomnia
  - long-term → ***trazodone***
  - acute → ***trazodone***; consider benzodiazepine (zolpidem, lorazepam)
- "Sundowning"
  - long-term → trazodone; consider risperidone, olanzapine, or CHAP
  - acute → trazodone; consider CHAP, risperidone, olanzapine
- Aggression or anger
  - severe, long-term → divalproex, risperidone, or CHAP
  - severe, acute → CHAP, risperidone
  - mild, long-term → divalproex, SSRI, trazodone, buspirone
  - mild, acute: → trazodone
- Osteoarthritic pain → tricyclic antidepressants, SSRIs, trazodone

IM Medications for Acute Interventions → ***haloperidol alone***; consider lorazepam alone

Managing Inadequate Response to Initial Medication

- Mild agitation
  - no response → ***switch to a second medication***
  - partial response → switch or combine
- Severe agitation
  - no response → ***switch to a second medication***
  - partial response → ***combine with a second medication***

Selecting the Next Medication after an Inadequate Response to:

- Conventional antipsychotic → ***atypical antipsychotic***; consider divalproex, trazodone, another conventional antipsychotic
- Atypical antipsychotic → conventional antipsychotic, another atypical antipsychotic; consider divalproex, trazodone, carbamazepine
- Benzodiazepines → atypical antipsychotic, conventional antipsychotic, divalproex, trazodone

Length of Trial to Determine Response

- For long-term treatment
  - antipsychotics and benzodiazepines: a few days to a few weeks.
  - buspirone, divalproex, antidepressants: minimum of 1–2 weeks up to 6 weeks
- For acute treatment → antipsychotics and benzodiazepines: approximately 2 days up to 1 week

When to Try Tapering If Good Response (approximate range of minimum and maximum treatment)

- Mild agitation:
  - antipsychotics and benzodiazepines: after 1–6 months
  - other medications: after 2–8 months
- Severe agitation
  - benzodiazepines: after 1.5–6 months
  - other medications: after 3–9 months

Safest Medications for Long-Term Use → ***SSRIs, buspirone***

Preferred Treatments by Clinical Situation, *continued*

Safest Medication Choices for Patients with High Medical Comorbidity

- Antipsychotics → risperidone
- Anxiolytics → buspirone
- Anticonvulsants → divalproex
- Antidepressants → SSRIs
- For sleep → trazodone

Medication Least Likely to Cause Drug Interactions → ***buspirone***

Agitation Executive Summary B: Consensus Recommendations by Somatic Treatments

Antipsychotics (***bold italics*** = first line)

- Conventional high potency antipsychotics
  - ***delirium (other than medication toxicity)***
  - ***long-term and acute management of agitation with psychosis***
  - long-term and acute management of agitation with severe anger or aggression
  - inadequate response to an atypical antipsychotic
  - inadequate response to a benzodiazepine
  - consider for long-term and acute management of agitation with "sundowning"
  - consider for inadequate response to another conventional antipsychotic
- Atypical antipsychotics
  - ***inadequate response to a conventional antipsychotic***
  - inadequate response to another atypical antipsychotic or to a benzodiazepine
  - Risperidone
    - ***long-term management of agitation with psychosis***
    - consider for long-term and acute management of agitation with sundowning
    - consider for long-term and acute management of agitation with severe anger or aggression
  - Olanzapine
    - consider for long-term and acute management of agitation with sundowning

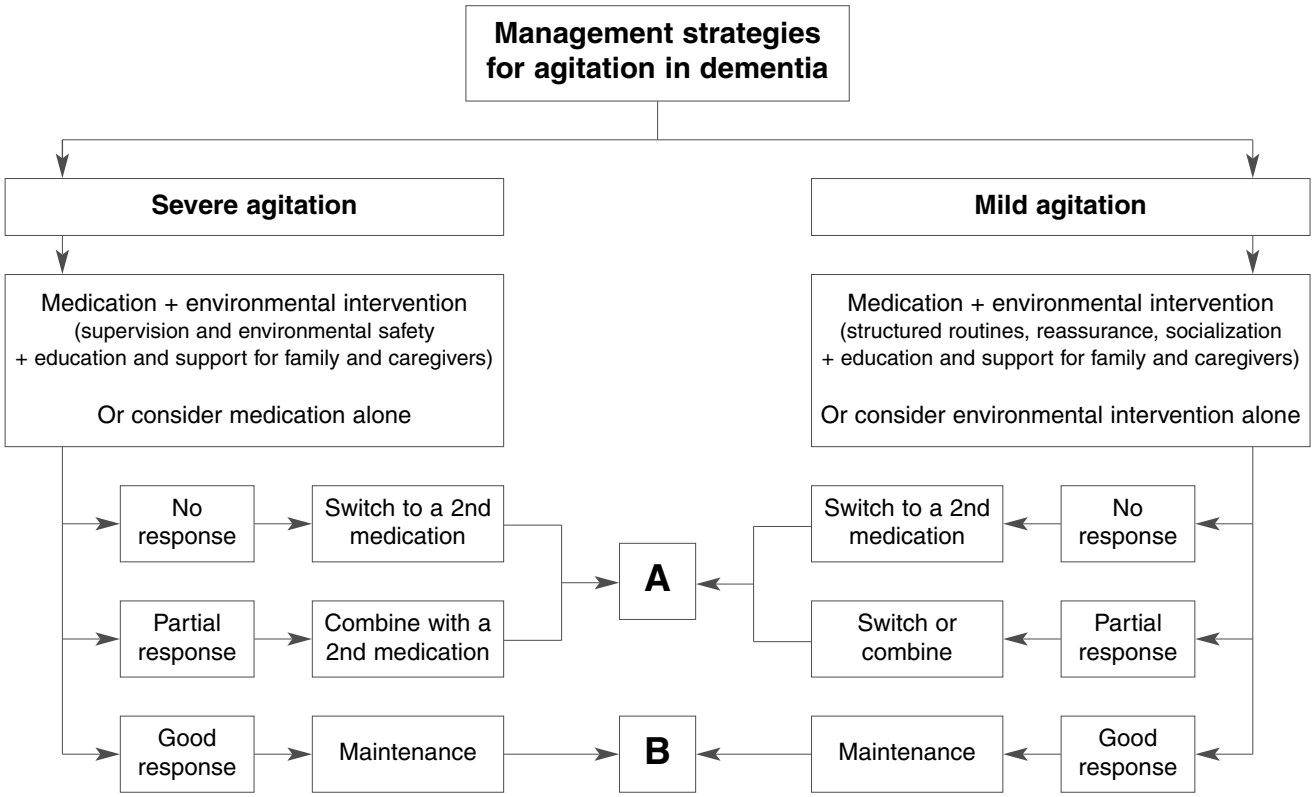
Antidepressants

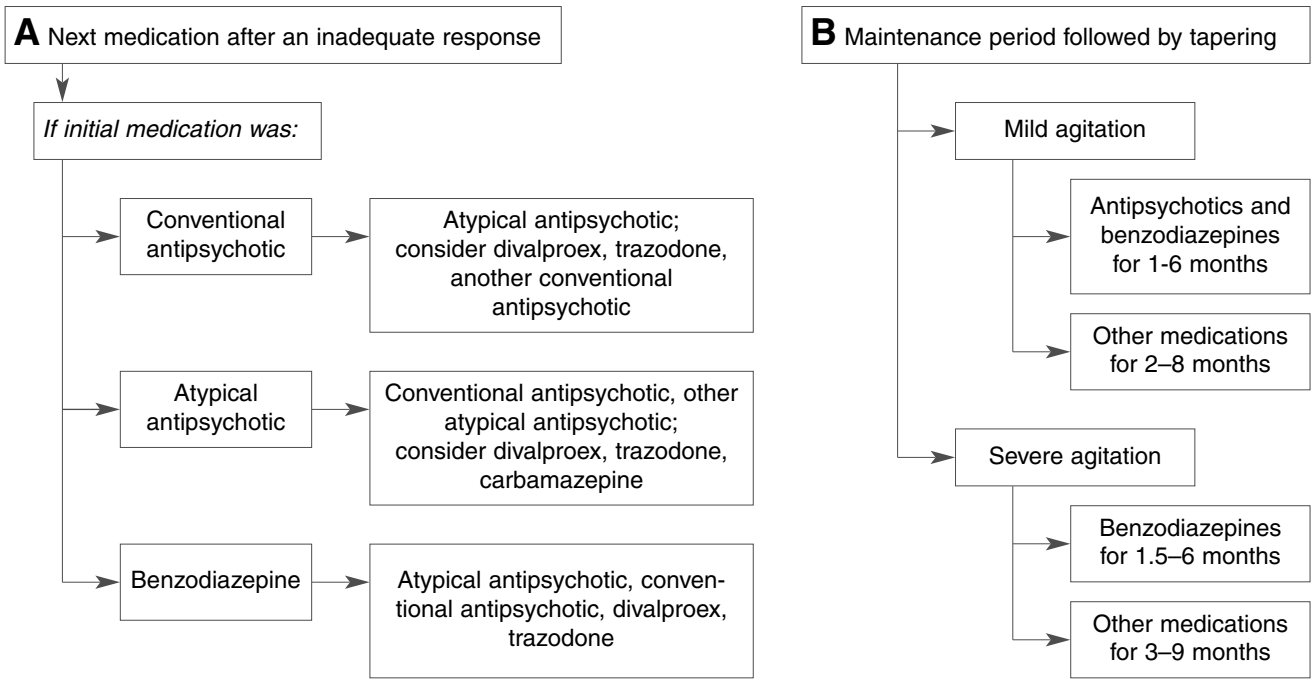
- SSRIs (sertraline and paroxetine preferred)
  - ***safe for long-term use in comparison with most other types of medication***
  - ***agitation with nonpsychotic depression; combine with antipsychotic for psychotic depression***
  - long-term management of agitation with mild anger
  - management of agitation due to osteoarthritic pain
- Trazodone
  - ***long-term and acute management of agitation with insomnia***
  - long-term and acute management of agitation with sundowning
  - long-term and acute management of agitation with mild anger
  - management of agitation due to osteoarthritic pain
  - inadequate response to a benzodiazepine
  - consider for inadequate response to a conventional or atypical antipsychotic
- Tricyclic antidepressants
  - management of agitation due to osteoarthritic pain

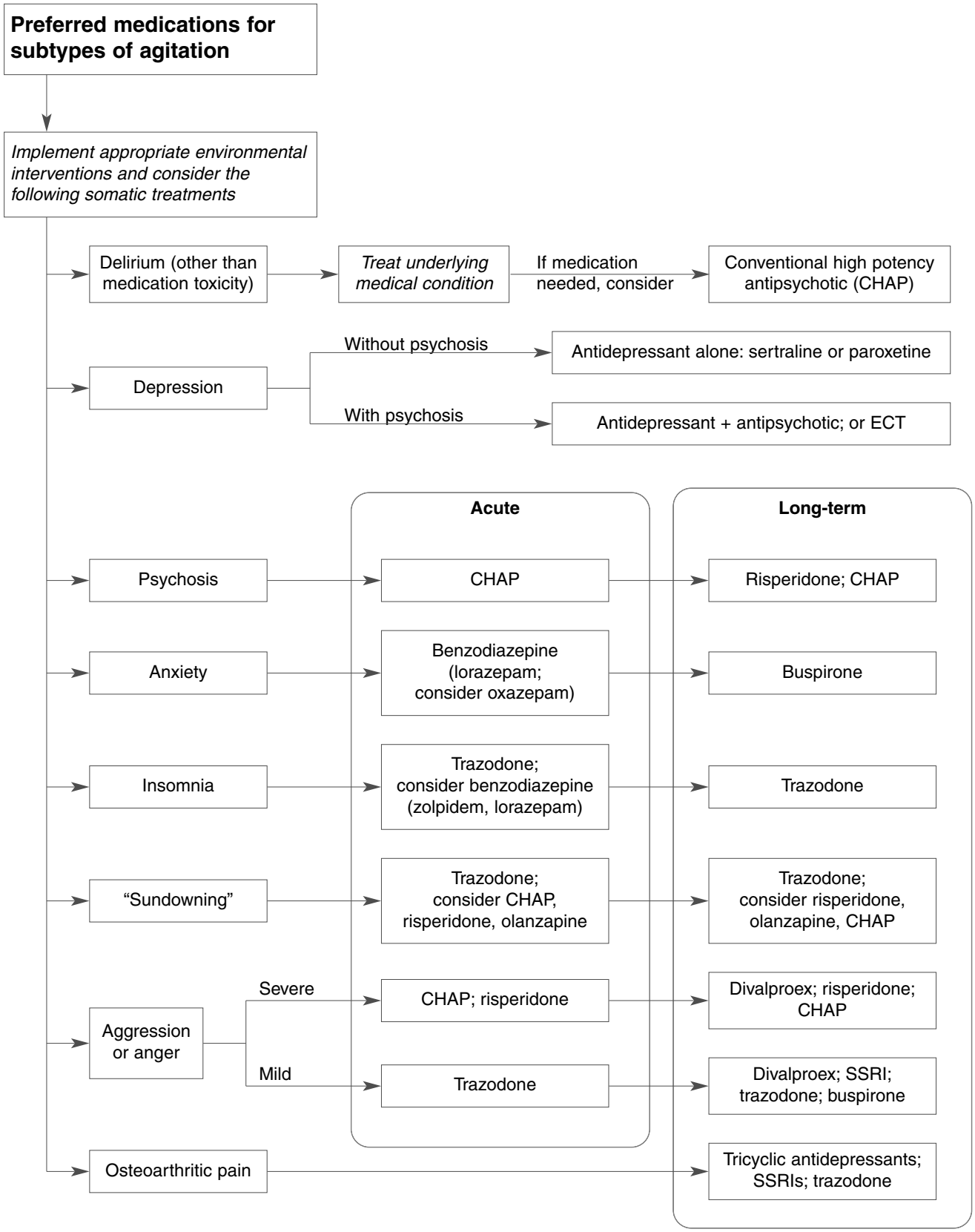
Other Treatments

- Benzodiazepines (lorazepam; consider oxazepam)
  - acute management of agitation with anxiety
  - consider for acute management of agitation with insomnia
- Buspirone
  - ***safe for long-term use in comparison with most other types of medication***
  - long-term management of agitation with anxiety
  - long-term management of agitation with mild anger
- Carbamazepine
  - ***agitation in a patient with comorbid seizure disorder***
  - consider for inadequate response to an atypical antipsychotic
- Divalproex
  - ***treatment of choice when using an anticonvulsant to control agitation***
  - ***agitation in a patient with comorbid seizure disorder***
  - long-term management of both mild and severe agitation with anger and aggression
  - inadequate response to a benzodiazepine
  - consider for inadequate response to a conventional or atypical antipsychotic
- Electroconvulsive therapy
  - ***agitation with psychotic depression***

Treatment Selection Algorithms



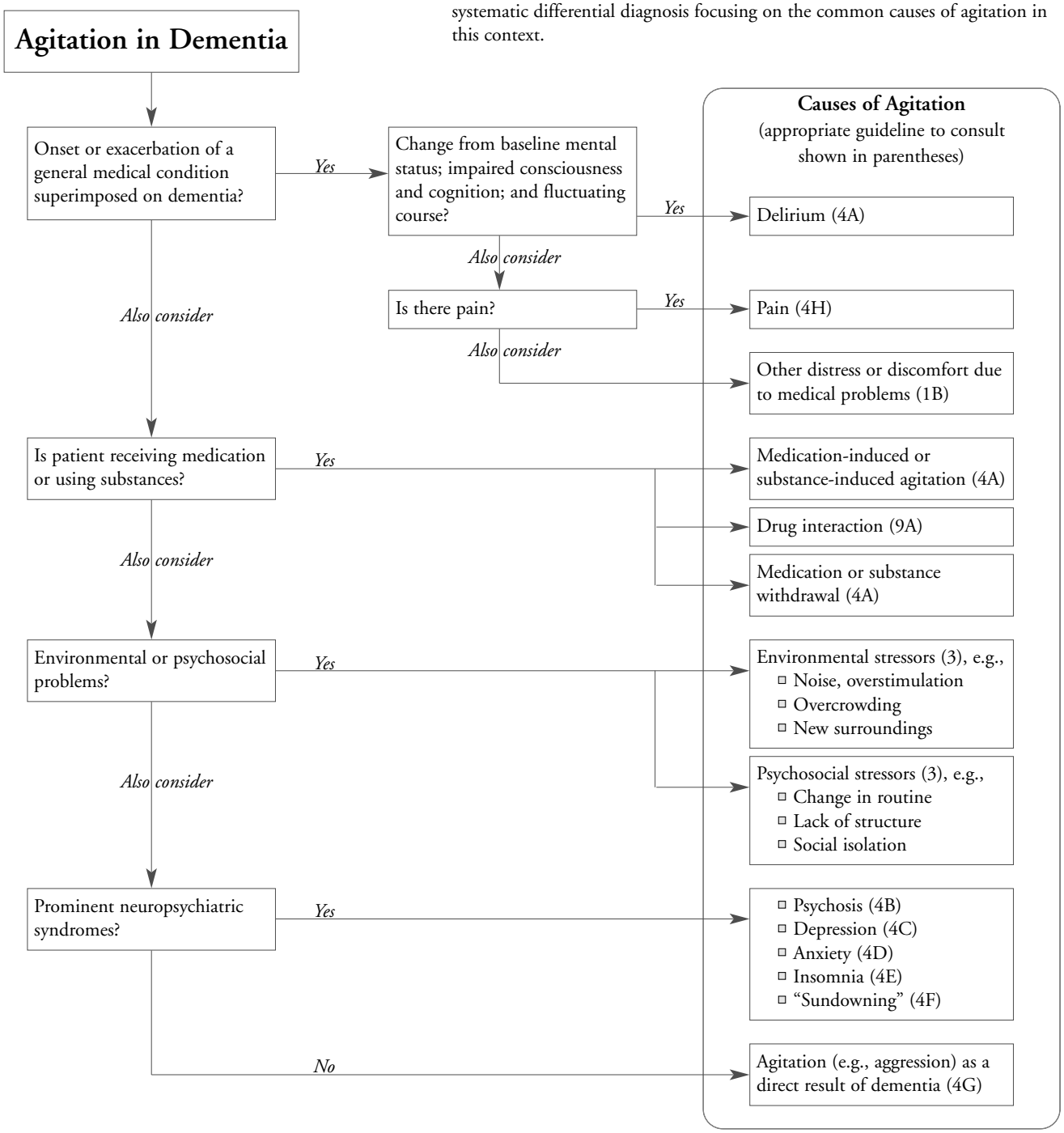



Preferred medications for subtypes of agitation
Implement appropriate environmental interventions and consider the following somatic treatments
Delirium (other than medication toxicity)
Treat underlying medical condition
If medication needed, consider
Conventional high potency antipsychotic (CHAP)
Depression
Without psychosis
Antidepressant alone: sertraline or paroxetine
With psychosis
Antidepressant + antipsychotic; or ECT
Acute
Long-term
Psychosis
CHAP
Risperidone; CHAP
Anxiety
Benzodiazepine (lorazepam; consider oxazepam)
Buspirone
Insomnia
Trazodone; consider benzodiazepine (zolpidem, lorazepam)
Trazodone
"Sundowning"
Trazodone; consider CHAP, risperidone, olanzapine
Trazodone; consider risperidone, olanzapine, CHAP
Aggression or anger
Severe
CHAP; risperidone
Divalproex; risperidone; CHAP
Mild
Trazodone
Divalproex; SSRI; trazodone; buspirone
Osteoarthritic pain
Tricyclic antidepressants; SSRIs; trazodone

Guideline 1: Assessment of Agitation in Dementia

1A. Differential Diagnosis

Introduction: Patients with dementia often have general medical illnesses and/or neuropsychiatric syndromes that may be responsible for their agitation. Therefore, before a treatment plan can be developed, it is crucial to conduct a systematic differential diagnosis focusing on the common causes of agitation in this context.



Guideline 1:* Assessment of Agitation in Dementia, *continued

1B. Medical Causes of Agitation in Dementia[1]

Summary: The experts recommend an exhaustive differential diagnosis to pursue potential underlying medical causes of change in mental status. The following conditions often cause delirium or agitation in patients with dementia.

	Priorities in Evaluation	Other Possibilities to Consider

General medical conditions to consider	▫ Medication-caused:
	  ▫ Drug interaction
	  ▫ Accidental misuse
	  ▫ CNS-toxic side effect*
	  ▫ Systemic disturbance (e.g., medication-induced electrolyte imbalance)
	▫ Urinary tract infection
	▫ Poor nutrition, decreased oral intake of foods and fluids
	▫ Respiratory infection
	▫ Recent stroke
	▫ Occult head trauma if patient fell recently
	▫ Pain*
	▫ Constipation*
		▫ Congestive heart failure
		▫ Orthostatic hypotension (e.g., low CNS blood flow if sitting for a long time)
		▫ Chronic obstructive pulmonary disease
		▫ Hypothyroidism
		▫ Diabetes
		▫ Current alcohol/substance-induced disorder
		▫ Alcohol/substance withdrawal
		▫ Occult long bone fracture if patient fell recently

Editors' Comment: It is also important to remember that agitation is often caused by more than one problem. The initial improvement following treatment of one underlying condition may not be sustained if another problem is also contributing. For example, a patient may be delirious due to a combination of congestive heart failure, drug-induced hyponatremia, and a drug interaction between an antiarrhythmic and an antidepressant medication.

[1]Question 1
*Editors' addition

Guideline 1:* Assessment of Agitation in Dementia, *continued

1C. Assessments and Diagnostic Tests[2]

Summary: In the assessment of agitation, the top priority of the expert panel is a careful bedside evaluation of the patient's psychiatric, general medical, neurologic, and cognitive status. The panel also recommends routine laboratory studies and serum drug levels for commonly used medications that can cause agitation if present in toxic levels. Additional more specific and specialized testing is recommended as needed after evaluation of the results generated from these screening efforts. (Note that this guideline is directed toward comorbid medical problems that may cause agitation, but does not cover the diagnostic workup for dementia itself.)

	Priorities to Perform (**bold** = assessment of choice)	**Consider as Needed**
Assessment	*At the bedside:* ▫ **Focused psychiatric history and examination** ▫ **General physical history and examination** ▫ **Routine cognitive examination and/or rating scale (e.g., Mini-Mental State examination*)** ▫ **Focused neurological examination** *Routine laboratory:* ▫ **Urinalysis** ▫ Complete blood count ▫ Sequential multichannel autoanalyzer (SMA) or similar chemistry screen *Serum drug levels if patient is taking:* ▫ Digoxin ▫ Anticonvulsant ▫ Theophylline ▫ Tricyclic antidepressant	▫ Thyroid-stimulating hormone (TSH) ▫ Electrocardiogram (ECG) ▫ Serum vitamin B_{12} (Cobalamin) ▫ Urine culture ▫ Chest x-ray ▫ Brain computed tomography (CT) scan ▫ Thyroid panel without TSH (T_4, T_3 uptake) ▫ Serum folate ▫ Brain magnetic resonance imaging (MRI) ▫ Toxicology screen (alcohol, drugs of abuse) ▫ Sedimentation rate

***Editors' Comment:** The Mini-Mental State examination (see *Appendix*, p. 38) provides a quick, quantitative measure of cognitive function and its change over time. Selected behavioral rating scales can also be useful (see *Suggested Readings*, p. 42, for references).

[2]Question 2

Guideline 2: Overall Management Strategies[3]

Introduction: Throughout the survey, we asked the experts to consider their strategies for treating agitation in four contexts: short- and long-term management of both mild and severe agitation. We used the following definitions:

Acute management — A drug or environmental intervention you would use for rapid symptom control over a period ranging from one time to a few weeks

Long-term management — A drug or environmental intervention you would use continuously for more than a few weeks (including chronic maintenance)

Mild agitation

- Behavior that is somewhat disruptive to others, but is nonaggressive and poses little risk of danger
- Caregivers feel taxed by the frequency of the behaviors and constant need for redirection

Examples: patient moans, cries, argues, paces, speaks inappropriately to strangers, asks repetitive questions, makes repetitive movements, uses telephone inappropriately, wanders but can be redirected

Severe agitation

- Aggressive or endangering behavior that is very disruptive and/or poses a threat of physical harm to self or others
- The agitation is a major source of difficulty to caregivers; commonsense verbal limit-setting and simple redirection by caregivers are ineffective

Examples: patient screams, insists on trying to leave dwelling or often gets lost in public places, makes feeding difficult, throws objects, grabs and scratches caregivers, bangs head or injures self

Summary: After pertinent medical conditions have been identified and managed (see *Guideline 1*), significant agitation may still be present and require intervention. The experts recommend that the treatment for agitation in dementia combine both medication and environmental intervention in almost all situations, regardless of the severity of the presentation or the length of treatment. This recommendation is especially important because there is often a tendency to neglect environmental interventions in formulating a treatment plan for such patients. For patients with mild agitation, the experts consider environmental intervention alone as sometimes sufficient (e.g., when there is no danger to safety; when the family or caregiver prefers to avoid medication; when the agitation is environmentally induced and the environment can be improved; or in patients at high risk for drug side effects or interactions). In severe agitation, medication alone is sometimes appropriate (e.g., if the patient is in danger or the environment cannot be changed).

	Mild Agitation		Severe Agitation	
	Long-Term Management	**Acute Management**	**Long-Term Management**	**Acute Management**
First line (**bold** = treatment of choice)	Environmental intervention *plus* Medication	Environmental intervention *plus* Medication	**Medication** ***plus*** **Environmental intervention**	**Medication** ***plus*** **Environmental intervention**
Highly rated second line	Environmental intervention alone	Environmental intervention alone	Medication alone	Medication alone

[3]Question 3

Guideline 3: Selecting Environmental Interventions[4]

Summary: As indicated in *Guideline 2*, the experts recommend that most patients receive some sort of environmental intervention. Agitated patients at any severity level may benefit from structure, individually targeted behavioral interventions, and education and emotional support for family and caregivers. Some interventions are more suitable depending on the degree of agitation. In mild agitation, several of the preferred strategies require active participation by the patient. In patients with severe agitation, interventions are more external, promoting safety and control of the environment. Behavioral interventions can be viewed as careful experiments: caregivers must often make educated guesses as to circumstances that trigger agitation, and sequential efforts to change selected elements in the environment may be necessary before the right formula is determined. Note that physical restraint is to be used very cautiously, generally only when agitation is severe and other efforts have failed. For a more detailed discussion of the types of behavioral intervention and education that may be helpful, refer to the *Guide for Families and Caregivers* (p. 81).

	Preferred Strategies (**bold** = intervention of choice)
For both mild and severe agitation	***Helping the family and caregivers*** ▫ **Educate about dementia and agitation** (see *Guide for Families and Caregivers*, p. 81) ▫ Encourage joining support groups ***Structuring the physical and psychosocial environment*** ▫ Provide a predictable routine for the patient ▫ Separate disruptive and noisy persons from quieter persons ▫ Control door access, use safety latches to prevent egress (most important in severe agitation) ***Behavioral interventions*** ▫ Reduce isolation; talk to agitated persons to distract them from frustration ▫ Identify specific precipitants to agitation ▫ Experiment with targeted changes to schedule and environment
Most important in ***mild*** agitation; sometimes consider in severe agitation	***Structuring the environment*** ▫ Use a night-light in bedroom during hours of sleep ▫ Provide orienting stimuli (e.g., clock, calendar, family pictures) ▫ Provide bright enough daytime lighting ***Behavioral interventions*** ▫ Provide reassurance and verbal efforts to calm ▫ If a patient wants to pace, allow it as long as there is no elopement risk ▫ Encourage pleasant experiences (e.g., recreation, pets, art)
Most important in ***severe*** agitation	▫ **Provide continuous supervision by an aide or relative** ▫ Rarely, and only in severe agitation, apply carefully monitored physical restraint (e.g., Posey)

[4]Question 4

Guideline 4: Selecting Medications for Specific Syndromes of Agitation

Organization of *Guideline 4*: *Guideline 4* is divided into eight sections that address medication choices for different neuropsychiatric presentations of agitation in dementia. We emphasize that the first consideration should always be treatment of comorbid general medical conditions (see *Guideline 1B*).

Clinicians should keep in mind that patients may have more than one cause for agitation. Treatments may need to be carefully sequenced, or sometimes combined, if multiple causes are present.

4A. Delirium[5]

Introduction: Delirium is a change in the patient's baseline mental status caused by a general medical condition, in which there is an impairment in the level of consciousness and cognition, often with a course that fluctuates rapidly over minutes or hours. Delirium indicates the presence of a medical emergency that can lead to death or worsening dementia. The underlying medical condition that is causing the delirium requires urgent identification and treatment. The agitation that accompanies delirium should receive separate treatment when it threatens the patient's safety, interferes with medical treatment (e.g., pulling out intravenous lines), or causes significant subjective distress. Unless agitation was present before the onset of delirium, the treatment for agitation in delirium is usually brief and the medication may be tapered when the medical condition has improved.

Summary: For delirium caused by common medical disorders, the experts prefer conventional high potency antipsychotics, followed closely by the atypical antipsychotics risperidone and olanzapine. Conventional antipsychotics may be preferred because they can be administered parenterally.

Common Causes of Delirium	First Line Medications	Also Consider
Congestive heart failure Urinary tract infection Upper respiratory infection Chronic obstructive pulmonary disease (COPD)* Pneumonia* Diabetes Dehydration or electrolyte imbalance Postoperative delirium†	Conventional high potency antipsychotic (e.g., haloperidol)	Risperidone Olanzapine
Medication (or substance) toxicity or interaction†	Reduce or stop offending medication; address substance use	
Benzodiazepine withdrawal†	Prescribe a benzodiazepine that has a short half-life and is metabolized well in older adults (e.g., lorazepam)	Prescribe a lower dose of whatever benzodiazepine the patient was previously using and taper slowly

***Further Recommendation:** The experts strongly recommend avoiding benzodiazepines in COPD or pneumonia.

[5]Question 5

†Editors' recommendations

Guideline 4:* Specific Syndromes of Agitation, *continued

4B. Psychosis[6]

Introduction: Psychotic symptoms in patients with dementia are often manifested as delusions related to forgotten recent events. For example, patients may misplace or forget where they put things and believe that someone has stolen them, or may believe that their spouse is having an affair because they don't recall seeing him or her for periods of time. Another common delusion is believing that family members or caregivers have been replaced by impostors. Hallucinations are less common and are not the same as confabulated delusional memories, such as reports of having seen nonexistent visitors or burglars at night (see *Guideline 4F*, "Sundowning").

Summary: For long-term treatment, the experts recommend risperidone, followed by conventional high potency antipsychotics. Extrapyramidal reactions and the long-term risk of tardive dyskinesia are potential concerns with conventional antipsychotics, especially at higher doses. The risks may be lower with risperidone. Olanzapine, divalproex, and trazodone are highly rated second line alternatives. For short-term treatment, the experts recommend conventional high potency antipsychotic medications, such as haloperidol, which have the advantage of being available in parenteral form for emergencies or for patients who cannot take oral medication. Atypical antipsychotics are highly rated second line choices for short-term use and are especially preferred in patients at high risk for extrapyramidal side effects. It should be noted that this expert survey was done before quetiapine and other newer atypical antipsychotics were available.

	Medication	
	Long-Term Management*	**Acute Management**
First line medications	▫ Risperidone ▫ Conventional high potency antipsychotic (e.g., haloperidol)	▫ Conventional high potency antipsychotic (e.g., haloperidol)
Also consider	▫ Olanzapine ▫ Divalproex ▫ Trazodone	▫ Risperidone ▫ Olanzapine

*See *Guideline 6B* for information on HCFA regulations regarding long-term use of antipsychotics.

Further Recommendations:

- For a patient whose agitation and psychosis occur in the context of dopamine agonist treatment for Parkinson's disease, the experts recommend olanzapine as the first line option, followed by clozapine and risperidone as second line options.[7]
- If the initial acute treatment is a conventional antipsychotic and the clinician then wishes to continue long-term treatment with a different medication, the conventional antipsychotic can usually be stopped or tapered quickly and the new medication started immediately.[†]

[6]Question 6 [7]Question 7 [†]Editors' recommendation

Guideline 4:* Specific Syndromes of Agitation, *continued

4C. Depression[8]

Introduction: Depressive symptoms in a patient with dementia are usually the same as those in younger patients but may be missed because they resemble the symptoms of a general medical illness (e.g., weight loss, sleep disturbance, fatigue) or dementia (e.g., flat affect, loss of interest, poverty of speech). In addition, depressive symptoms in a patient with dementia may fluctuate widely over short periods of time and may not meet the full criteria for a major depressive episode. Depression can be very hard to separate from apathy and anhedonia secondary to dementia, a picture where the role of antidepressants is less clear. The presence of depressed mood is often what makes the syndrome clearer.The clinician should evaluate for vegetative symptoms (e.g., poor sleep or appetite), nonverbal signs of depressed mood (e.g., facial expression of suffering and sadness, sobbing), and verbally expressed feelings of hopelessness, helplessness, or guilt. Depression with psychosis may be characterized by delusions of guilt, impoverishment, jealousy, and persecution.

Summary: The treatment of prominent depressive symptoms in an elderly patient with dementia and agitation will vary depending on the severity of the depression and whether psychotic symptoms are present. For mild to moderate depression, the experts first line choice is an antidepressant alone, but there is also modest support for adding psychotherapy. For severe depression without psychosis, the treatment of choice is an antidepressant alone, but electroconvulsive therapy (ECT) should also be considered. For severe depression with psychosis (often called delusional depression), the combination of antidepressant and antipsychotic medication is the treatment of choice, and ECT is also a first line option.

	Mild to Moderate Depression	**Severe Depression, No Psychosis**	**Severe Depression with Psychosis**
First line strategies (**bold** = treatment of choice)	Antidepressant alone*	**Antidepressant alone***	**Antidepressant* + antipsychotic** ECT†
Also consider	Some experts suggest adding psychotherapy to the antidepressant	ECT†	

*See *Guideline 7* for details on selecting specific antidepressants.

†**Editors' Comment:** ECT may cause more severe and persistent memory loss and other cognitive impairments in a patient with dementia than in a nondemented patient; however, this complication eventually subsides.

[8]Question 8

Guideline 4:* Specific Syndromes of Agitation, *continued

4D. Anxiety[9]

Introduction: Generalized anxiety presents with verbal or facial expressions of worry, nervousness, or fear and/or somatic symptoms such as palpitations, stomach problems, or feelings of tension. Patients may repeatedly request reassurance or complain of somatic symptoms. Worries are often related to memory loss, such as needing repeated assurance that loved ones are safe or are planning to visit, that belongings have not been lost, or that plans and schedules will be kept.

Summary: For long-term management, the experts prefer buspirone, with trazodone and the selective serotonin reuptake inhibitors (SSRIs) as alternatives. For acute treatment, the experts prefer benzodiazepines. However, for safety reasons, benzodiazepines are not recommended for long-term use (see also *Guideline 7*).

	Long-Term Management*	**Acute Management**
Preferred medications (none were first line)	Buspirone	Benzodiazepine†
Also consider	Trazodone Selective serotonin reuptake inhibitor (SSRI)†	Trazodone

*See *Guideline 6B* for HCFA regulations.

†See *Guideline 7* for details on selecting a specific benzodiazepine or a specific SSRI.

Further Recommendation: Buspirone and the SSRIs have a gradual onset of action. If the initial acute treatment is a benzodiazepine and the clinician then wishes to continue long-term treatment with buspirone or an SSRI, either can be added while the benzodiazepine is tapered.‡

[9]Question 9

‡Editors' recommendation

Guideline 4:* Specific Syndromes of Agitation, *continued

4E. Insomnia[10]

Introduction: Insomnia is a common source of distress in the elderly who often sleep less and have reduced sleep efficiency as part of the aging process. Insomnia may also be due to an identifiable cause that should be treated appropriately, such as pain or distress associated with a general medical condition, psychosis, depression, or anxiety.

Summary: The experts prefer trazodone for both long-term and acute treatment of nonspecific insomnia. Benzodiazepines are acceptable as second line only for short-term use.

	Long-Term Management	**Acute Management**
First line medications	Trazodone*	Trazodone*
Also consider	(Other medications very cautiously)	Benzodiazepine†

*Some expert panel members suggested nefazodone as well, a related compound that we did not include in the survey as an option for insomnia.

†See *Guideline 6B* regarding HCFA regulations and *Guideline 7* for details on selecting a specific benzodiazepine or other sedative-hypnotic medication.

Editors' Recommendation: Clinicians should also consider the principles of sleep hygiene (e.g., reduce daytime caffeine; avoid nocturia by reducing fluid intake in the evening; reduce noise level; adjust lights up or down as needed; provide a soothing activity before bed; have the patient spend less time in bed to match the actual need for sleep).

[10]Question 10

4F. "Sundowning"[11]

Introduction: Sundowning consists of agitation, confusion, and disorientation that often start in the late afternoon and become especially severe at night. It may be the result of a number of causes, including fatigue, loss of visual cues in the dark, and instability in circadian rhythm. Sundowning may result in dangerous behavior such as falls from wandering or climbing over bed rails. It may be helpful to use orienting environmental interventions such as night-lights or reassuring check-ins from caregivers. Medication can help promote sleep and diminish confusion.

Summary: The experts recommend first trying trazodone for both long-term and acute management. Should this fail, antipsychotics are recommended. If long-term use is necessary, atypical antipsychotics are preferred over conventional antipsychotics.

	Long-Term Management	**Acute Management**
Preferred medications (none were first line)	▫ Trazodone	▫ Trazodone
Also consider	▫ Risperidone ▫ Olanzapine ▫ Conventional high potency antipsychotic	▫ Conventional high potency antipsychotic ▫ Risperidone ▫ Olanzapine

[11]Question 11

Guideline 4:* Specific Syndromes of Agitation, *continued

4G. Aggression or Anger Not Due to Other Causes (e.g., Psychosis, Depression, Anxiety, Insomnia)[12]

Introduction: This guideline deals with aggression or anger that is not primarily explained by another syndrome such as psychosis or anxiety. *Mild anger* (i.e., without physical aggression) may be limited to specific situations (e.g., bathing, getting out of bed) or may be continuous. *Severe anger with physical aggression* is characterized by acts directed at caregivers and other people (e.g., forcefully pushing away a hand offering food; pushing, slapping, or scratching; extremely loud and disruptive yelling for extended periods).

Summary: The experts made no first line recommendations. For *mild anger*, the experts prefer divalproex or serotonergic medications (SSRIs, trazodone, buspirone) for long-term treatment and trazodone for acute treatment. For the long-term treatment of *severe anger with physical aggression*, they favor divalproex, followed by risperidone or conventional high potency antipsychotics. For acute treatment, they favor conventional high potency antipsychotics or risperidone, both of which work rapidly.

	Mild Anger, Not Aggressive		Severe Anger with Physical Aggression	
	Long-Term Management	**Acute Management**	**Long-Term Management**	**Acute Management**
Preferred medications (none were first line)	Divalproex Selective serotonin reuptake inhibitor (SSRI)* Trazodone Buspirone	Trazodone	Divalproex Risperidone† Conventional high potency antipsychotic†	Conventional high potency antipsychotic Risperidone
Also consider	*Only modest support for:* Carbamazepine Risperidone† Olanzapine†	*Only modest support for:* Benzodiazepine Conventional high potency antipsychotic Risperidone	Olanzapine† Carbamazepine Trazodone SSRI*	Olanzapine Trazodone

*See *Guideline 7* for details on selecting a specific SSRI.
†See *Guideline 6B* regarding HCFA regulations for long-term use of antipsychotics.

Further Recommendations:

- If the initial acute treatment is a conventional antipsychotic and the clinician then wishes to continue long-term treatment with a different medication, one of the preferred long-term choices (divalproex or risperidone) can be added while the conventional antipsychotic is stopped or tapered.‡
- Divalproex might be preferred in aggressive patients without prominent psychosis, while antipsychotics might be considered more strongly in patients with prominent psychosis. Divalproex may also be used as an adjunct to antipsychotics in psychotic patients who continue to be severely aggressive (see *Guidelines 5A* and *5B*).‡
- Since anger in dementia may be the result of feeling overwhelmed by or misinterpreting the environment, it can be very helpful to simplify and structure surroundings and ensure that they are well lighted, reduce noise levels, follow a more predictable routine, and reduce distractions.‡

[12]Question 12

‡Editors' recommendation

Guideline 4: **Specific Syndromes of Agitation,** ***continued***

4H. Prominent Pain[13]

Introduction: Musculoskeletal pain from chronic osteoarthritis is a common problem that is often resistant to drug therapy. Comfortable positioning, physical therapy, local heat, and other pain management techniques can be helpful. Treatment with acetaminophen or nonsteroidal anti-inflammatory drugs should also be tried. Despite these measures, patients may become agitated due to continued pain and may benefit from treatment with certain psychotropic medications.

Summary: The experts had no first line recommendations, but preferred tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs), and trazodone over codeine compounds when dealing specifically with agitation.

Preferred medications (none were first line)	Tricyclic antidepressant Selective serotonin reuptake inhibitor Trazodone

[13]Question 13

Guideline 5: Managing Inadequate Response to Medication

Introduction: Before changing or adding medication in a patient who is having no response or only a partial response, it is important to consider the following questions and take appropriate action:

1. Has the medication been given for an adequate duration and at an adequate dose (see *Guidelines 5C* and *8*)?
2. Are medication side effects or drug interactions causing problems?
3. Is the medication being taken as prescribed?
4. Have environmental stressors been evaluated and altered?
5. Have underlying medical disorders and delirium been ruled out or treated?
6. Have neuropsychiatric syndromes related to dementia (e.g., psychosis, depression, anxiety) been properly identified and treated with recommended medications?
7. If degree of response is uncertain or fluctuating, have you considered using a rating scale to objectively document change? (See *Suggested Readings*, p. 42, for a list of representative scales.)

5A. Should You Switch Medication or Combine?

Summary: The experts usually avoid polypharmacy in this vulnerable patient group, preferring to use drugs one at a time in most situations. In mild or severe agitation with no response to the first drug, the experts clearly prefer switching to a new medication. In severe agitation, however, the experts support adding a second medication if the patient has had a partial response to the first, since the recurrence of full-blown agitation may be more dangerous than the potential risk of drug interactions. In mild agitation with partial response to the first drug, the experts have no first line recommendation and support either switching or combining. When combinations are chosen, care should be taken to select new medications that will not interact negatively with those already being taken (see *Guidelines 5B* and *9A* for safer combinations).

Editors' Comment: Should a drug combination be needed, the clinician can lessen the risk of drug interactions by trying lower doses of each agent rather than the usual "full" doses for single-drug therapy.

	Mild Agitation		**Severe Agitation**	
	No Response[14]	**Partial Response**[15]	**No Response**[14]	**Partial Response**[15]
First line	Switch to a second medication	*No first line recommendation*	Switch to a second medication	Combine with a second medication
Second line	(Combinations generally not preferred)	Switch to a second medication Combine with a second medication	Combine with a second medication	Switch to a second medication

Editors' Recommendation: Should a patient improve when two drugs are combined, the clinician may wish at some future point to taper one of the medications slowly to find out if a single medication alone will be sufficient.

[14]Question 14 [15]Question 15

Guideline 5:* Managing Inadequate Response to Medication, *continued

5B. Selecting the Next Medication

Summary: For patients who have not responded adequately to conventional antipsychotics (e.g., haloperidol), the experts recommend switching to an atypical antipsychotic. Divalproex, trazodone, or another conventional antipsychotic are second line alternatives. For patients who have not responded adequately to an initial trial of an atypical antipsychotic, the experts recommend switching to a conventional antipsychotic, if this has not been previously tried, or to another atypical antipsychotic (e.g., risperidone to olanzapine or vice versa). For patients who have not responded adequately to a trial with a benzodiazepine, the next step would be an antipsychotic, divalproex, or trazodone. When the clinician wishes to add a second drug to an antipsychotic, either to augment a partial response or because single-drug trials have failed, divalproex or trazodone is generally preferred as an add-on. If a patient is receiving ongoing treatment with a benzodiazepine and a second drug is needed, the preferred choice is an antipsychotic or divalproex. The experts recommend using benzodiazepines for immediate p.r.n. use when extra sedation is needed in patients on antipsychotics. Antipsychotics are recommended for p.r.n. use in patients on benzodiazepines.

Editors' Comment: In choosing the second medication, it can be helpful to focus on the main symptoms being treated (e.g., switch to antipsychotics for prominent psychosis, divalproex for prominent aggression, trazodone for uncomplicated insomnia). If the initial switching strategy fails, the other choices may be tried.

	If Switching		If Combining	
Previous Medication	**Preferred Agents** (none were rated first line except where indicated)	**Also Consider**	**Consider for Ongoing Treatment***	**Preferred for P.R.N. Use†**
Conventional antipsychotic[16]	▫ Atypical antipsychotic (first line)	▫ Divalproex ▫ Trazodone ▫ Another conventional antipsychotic	▫ Divalproex ▫ Trazodone	▫ Benzodiazepine
Atypical antipsychotic[17]	▫ Conventional antipsychotic ▫ Another atypical antipsychotic	▫ Divalproex ▫ Trazodone ▫ Carbamazepine	▫ Trazodone ▫ Divalproex	▫ Benzodiazepine
Benzodiazepine[18]	▫ Atypical antipsychotic ▫ Conventional antipsychotic ▫ Divalproex ▫ Trazodone	▫ Carbamazepine ▫ Antidepressant	▫ Conventional or atypical antipsychotic ▫ Divalproex	▫ Antipsychotic

*There was little consensus on combination strategies. Their main use is in severe agitation when there has been a partial response to the first medication (see *Guideline 5A*).

Further Recommendations:

- ▫ When switching from an antipsychotic, if there has been a partial response, the antipsychotic should be tapered while starting the new agent. However, if there has been no response to the antipsychotic, it may be stopped altogether when the new drug is started.‡
- ▫ Benzodiazepines should be tapered when switching to a new drug, unless they have been prescribed at extremely low doses (e.g., lorazepam 0.25–0.5 mg at bedtime).‡

†Editors' recommendations, adapted from Question 19
‡Editors' recommendation
[16]Question 16
[17]Question 17
[18]Question 18

Guideline 5: **Managing Inadequate Response to Medication,** ***continued***

5C. Defining Inadequate Response: How Long to Try a Medication

Introduction: Agitation in dementia is often a chronic problem requiring long-term management and it may take many weeks of treatment at gradually adjusted doses to determine if a given medication and dosage schedule are useful. Sometimes, very brief use of medication may be helpful to stabilize a patient during an acute crisis.

1. For longer-term management[19]

Summary: Among medications used to treat agitation, some work rapidly while others have a delayed onset of action. The experts generally recommend trials of 2 weeks or longer for divalproex, buspirone, and antidepressants. Antipsychotics, trazodone, and benzodiazepines may produce a response in 1 week or less.

	How Long to Try a First Medication Before Switching to or Adding Another Medication If Response Inadequate	
Medication	**Shortest**	**Longest (weeks)**
Antipsychotic (atypical or conventional)	4–7 days	2–4
Benzodiazepine	3–4 days	1–3
Buspirone	1.5–2.5 weeks	4–6
Divalproex	1–2 weeks	3–6
Selective serotonin reuptake inhibitor	10–14 days	4–6
Tricyclic antidepressant	10–14 days	4–6
Trazodone	7–10 days	3–4

2. In an acute situation[20]

Summary: To determine if a medication will be helpful in an acute situation, the experts recommend trying an antipsychotic for at least 2 or 3 days and a benzodiazepine for at least 1 or 2 days. If the response to the initial treatment is not adequate, the clinician should wait no longer than 1 week before deciding on the next step.

	How Long to Try a First Medication Before Switching to or Adding Another Medication If Response Inadequate	
Medication	**Shortest (days)**	**Longest (days)**
Antipsychotic (atypical or conventional)	2–3	6–8
Benzodiazepine	1–2	4–6

[19]Question 20

[20]Question 21

Guideline 6: Long-Term Treatment Issues

6A. Medications for Long-Term Safety[21]

Summary: It is important to monitor the long-term safety of continuous psychotropic medication use in elderly patients, both as general practice and specifically to comply with HCFA requirements for long-term care facilities. The experts indicate that selective serotonin reuptake inhibitors (SSRIs) and buspirone are least likely to cause serious problems with continued long-term use. Other drugs require more careful monitoring. The experts rate the newer antidepressants, such as bupropion, nefazodone, and venlafaxine, as less safe than the SSRIs but considerably safer than the tricylic antidepressants (e.g., amitriptyline). Among anticonvulsants, divalproex is preferred over carbamazepine. Atypical antipsychotics are viewed as considerably safer than conventional antipsychotics.

	Medication	Comment
First line	▫ Selective serotonin reuptake inhibitor	▫ Preferred over other antidepressants and strongly preferred over the tricyclic antidepressants (TCAs)
	▫ Buspirone	▫ Among anxiolytics, strongly preferred over benzodiazepines
Second line	▫ Divalproex	▫ Among anticonvulsants, preferred over carbamazepine
	▫ Other newer antidepressant (e.g., bupropion, mirtazapine, nefazodone, venlafaxine)	▫ Among antidepressants, preferred over TCAs
	▫ Atypical antipsychotic (other than clozapine)	▫ Strongly preferred over conventional antipsychotics

[21]Question 22

Guideline 6: **Long-Term Treatment Issues,** ***continued***

6B. When to Taper Medication If the Patient Has Had a Good Response

Summary: Although some patients require long-term treatment, it is important periodically to taper and try to discontinue medication following a period of satisfactory improvement. In general, the experts suggest attempting to taper medication as soon as 2 to 3 months, particularly in milder agitation, and certainly within 6 to 9 months even in a patient who had severe agitation. The recommended period of treatment tends to be somewhat shorter for antipsychotics and especially for benzodiazepines. Repeated relapses suggest the need for continuing medication indefinitely.

Editors' Comment: In deciding whether to continue or taper medication for agitation, the editors recommend considering the following factors:

- For patients in nursing homes, clinicians should consult HCFA Long Term Care Guidelines,* which are briefly summarized here:
  - Benzodiazepines and other sedative-hypnotics for sleep: If used for more than 10 continuous nights, gradual dose reduction should be attempted at least three times within 6 months before concluding that the dose reduction is contraindicated.
  - Benzodiazepines and other anxiolytics (excluding buspirone) for uses other than to promote sleep: gradual dose reduction should be attempted at least twice within 1 year before concluding that the gradual dose reduction is contraindicated.
  - Antipsychotics: Gradual dose reductions should be attempted at least twice within 1 year unless the patient has had psychotic symptoms (hallucinations or delusions) that have stabilized on medication and that are due to dementia or another psychiatric disorder.
  - Antidepressants: There are no time points for discontinuation, only a requirement for documentation of the rationale for continued use.
  - Behavioral monitoring charts are recommended to document continued need for medication.
- If response is uncertain, have you considered using behavioral monitoring charts as an objective aide to document the level of agitation and the effects of medication and help rule out incidental fluctuations? (See *Suggested Readings*, p. 42, for a list of selected rating scales.)

	Length of Time to Treat Before Trying to Taper and Discontinue[22]			
	Mild Agitation		Severe Agitation	
Medication	**Fewest Months**	**Most Months**	**Fewest Months**	**Most Months**
Antidepressant (not for depression)	2–3	6–8	3–4	7–9
Antipsychotic (atypical or conventional)	1.5–2	4–6	2–3	6–8
Benzodiazepine	1–2	3–6	1.5–2	4–6
Buspirone	2–3	5–8	2.5–4	6–9
Divalproex	2–3	6–8	3–4	7–9
Trazodone	2–3	6–8	2.5–4	7–9

Further Recommendations: Tapering should be done gradually (e.g., 25% every week or two). Most of the experts do not recommend continuing medication indefinitely, especially in milder agitation.

*Department of Health and Human Services, Health Care Financing Administration. Long Term Care Guidelines. Transmittal No. 274, June 1995 (see p. 39 for information on requesting a copy)

[22]Question 23

Guideline 7: Selecting Specific Medications within Different Classes of Drugs

Summary: Individual medications even within a given group may vary considerably in tolerability, efficacy, and the risk of interaction with other drugs. Among antidepressants, the experts recommend sertraline or paroxetine as first line choices, with nortriptyline, venlafaxine, and fluoxetine as the top-rated second line alternatives. Lorazepam and buspirone are preferred over the other anxiolytics for agitation. Zolpidem and lorazepam are preferred among sedatives for sleep—both have intermediate half-lives (8–12 hours) and simple metabolism. Divalproex is the treatment of choice among anticonvulsants for use in agitation.

	Preferred Agents (**bold** = treatment of choice)	**Also Consider**
Antidepressant[23]	Sertraline (first line) Paroxetine (first line)	*Top second line choices bordering first line:* Nortriptyline Venlafaxine Fluoxetine *Other highly rated second line choices:* Nefazodone Desipramine Trazodone Bupropion Fluvoxamine
Anxiolytic for generalized daytime agitation (none were first line)[24]	Lorazepam Buspirone	Oxazepam
Sedative-hypnotic or anxiolytic to promote sleep (none were first line)[25]	Zolpidem Lorazepam	Temazepam Oxazepam Chloral hydrate
Anticonvulsant[26]	**Divalproex**	Carbamazepine (highly rated second line) Gabapentin

Further Recommendation: The choice of a specific antipsychotic agent is dependent on the nature of the presentation and whether the management situation is acute or long-term. Refer to *Guideline 4* for recommendations about factors that influence this selection.

[23]Question 24
[24]Question 25
[25]Question 25
[26]Question 26

Guideline 8: Dose[27] and Side Effects

Summary: Manufacturers' dosing recommendations are usually intended for younger patients. Dosages for the drugs shown below are much lower for elderly than for younger patients. The starting doses recommended by the expert consensus panel may be sufficient in many cases, but doses can be gradually increased toward the target dose based on the clinician's judgment of how well the patient is responding to and tolerating the medication. The highest doses should be reserved only for patients who have not responded to lower doses but are tolerating those doses well. The editors list the most common or important side effects and refer readers to comprehensive references such as the *Physicians' Desk Reference* (see p. 41) and *Drugs of Choice from the Medical Letter* (see p. 40) for more complete information.

Medication	Recommended Oral Doses (mg/24 hr)			Most Important Side Effects[a]
	Starting Dose	Average Target Dose	Highest Final Dose	
Buspirone (Doses usually divided b.i.d.)	10	30	50–60	Headache, dizziness, nausea; rarely overstimulation
Divalproex (Doses usually divided b.i.d.)	250–375	625–825	1250–1750	Nausea, tremor, weight gain, hair loss, thrombocytopenia, drowsiness, rarely hepatic dysfunction
Divalproex blood level	20–50 *mcg/ml*	50–85 *mcg/ml*	80–120 *mcg/ml*	
Carbamazepine	100–200	400–600	800–1000	Rash, drowsiness, blurred or double vision, headache, ataxia, nausea, mild leukopenia, rare agranulocytosis
Carbamazepine blood level	2–5 *mcg/ml*	7–8 *mcg/ml*	10–11 *mcg/ml*	
Haloperidol[b]	0.5–1.0	1.5–2.0	5–7	Drowsiness, postural hypotension, extrapyramidal effects (EPS), tardive dyskinesia, weight gain, anticholinergic effects[c]
Lorazepam[b]	0.5–1.5	1.5–2.5	3–5	Drowsiness, ataxia, amnesia, disinhibition, paradoxical excitement, depression, dizziness, withdrawal symptoms, rebound insomnia or excitement
Olanzapine	2.5–5.0	5.0–7.5	12.5–15	Drowsiness, weight gain, dizziness, anticholinergic effects, postural hypotension, EPS (rare)
Risperidone[d]	0.25–0.5	0.5–1.5	2–3	Blurred vision, dizziness, drowsiness, postural hypotension, headache, nausea, EPS (occasional), weight gain (occasional)
Trazodone	25–50	50–100	250–300	Drowsiness, headache, GI upset, occasional postural hypotension and ventricular arrhythmias, priapism in men (rare)

Editors' Note: Antidepressants are not covered in this table because of the complexity of the subject. Appropriate doses of selective serotonin reuptake inhibitors for elderly patients vary widely. Tricyclic antidepressants should only be used with careful monitoring of blood levels.

[a]Abramowicz M, ed. Drugs of choice from the Medical Letter. New Rochelle, NY: Medical Letter, Inc; 1997

[b]Fluphenazine is also frequently used, with approximately the same dose ranges as for haloperidol. For IM injection of haloperidol alone, the experts recommend a dose of 0.7-2.4 mg. For IM injection of lorazepam alone, they recommend a dose of 0.5-1.5 mg. Although not generally recommended, when the clinician feels it is necessary to combine haloperidol and lorazepam in an IM injection, the experts recommend using the lower end of the IM dose range for both drugs.[28]

[c]Anticholinergic effects are defined by the *Drugs of Choice from the Medical Letter* as dry mouth, mydriasis, cycloplegia, urinary retention, constipation, tachycardia, memory impairment, and delirium.

[d]Editors' recommendations; doses shown are lower than those suggested by the expert panel, reflecting new data that became available after the survey was conducted (Janssen Pharmaceutica, on file).

[27]Question 27

[28]Questions 27 and 28

Guideline 9: Safety and Tolerability

9A. Medications Least Likely to Cause Drug Interactions[29]

Introduction: Watching out for drug interactions is a high priority in older patients for at least four reasons: 1) older patients usually metabolize drugs more slowly than younger patients; 2) this population is often on multiple medications, increasing the likelihood of having an adverse interaction; 3) older patients are often more frail and therefore may be more sensitive to the adverse consequences of an untoward interaction; and 4) ironically, drug interactions may be misidentified and mistakenly attributed to an underlying medical illness. There are two types of interactions. A *pharmacokinetic* interaction is the alteration by one drug of the absorption, distribution, metabolism, or elimination of another drug. A major example is the inhibition of hepatic cytochrome P450 (CYP) isoenzymes by various selective serotonin reuptake inhibitors (SSRIs), which may increase the levels of other medications metabolized by these enzymes. A *pharmacodynamic* interaction is the alteration by one drug of the nature or magnitude of the response to another drug because of the first drug's effects on the second drug's site of action. An example would be additive diarrhea in a patient receiving both an SSRI and a laxative.

Summary: The experts rated buspirone as the first line choice to avoid drug interactions. Highly rated second line choices are the antidepressants sertraline, bupropion, venlafaxine, paroxetine, and nefazodone; atypical antipsychotics; high potency conventional antipsychotics; and divalproex. We have highlighted a few key interactions for each medication; clinicians are advised to check the *Physicians' Desk Reference* (see p. 41) or other similar sources for comprehensive lists of specific interactions caused *by* and *to* each medication.

	Medication	Editors' Comment
First line	Buspirone	Metabolized by CYP3A; its level may be raised by CYP3A inhibitors (e.g., ketaconazole, macrolide antibiotics, nefazodone). Is not known to alter CYP enzymes itself, but has not been extensively studied in this regard. Use cautiously with other drugs that may cause nausea.
Higher second line, less problematic (drugs in each class are listed in order of mean scores; differences were not statistically significant)	***Antidepressants***	
	Sertraline	Modest inhibition of CYP2D6 at higher doses. Examples of substrates whose levels may be increased: tricyclic antidepressants, many opiates, antiarrhythmics, and beta-blockers.
	Bupropion	Lowers seizure threshold; use cautiously with other drugs that do the same. Levels of hydroxybupropion (major active metabolite) may be raised by CYP2D6 inhibitors (e.g., fluoxetine). Is not known to alter CYP enzymes itself, but has not been extensively studied in this regard.
	Venlafaxine	Modest inhibition of CYP2D6; also potential for increased venlafaxine level if combined with other inhibitors of CYP2D6. May raise blood pressure so that increased dose of antihypertensive medication may be needed.
	Paroxetine	Substantial inhibition of CYP2D6; will increase levels of 2D6 substrates.
	Nefazodone	Substantial inhibition of CYP3A at higher doses. Examples of substrates whose levels may be increased: tricyclic antidepressants, sertraline, acetaminophen; many calcium blockers, antiarrhythmics, benzodiazepines, and opiates.
	Atypical and high potency conventional antipsychotics	May exacerbate sedation or hypotension caused by other medications; potential additive akathisia or extrapyramidal symptoms with SSRIs. Haloperidol (and perphenazine, a medium potency antipsychotic) moderately inhibits CYP2D6. Effects of atypical antipsychotics on CYP enzymes are not well known.
	Anticonvulsant	
	Divalproex	Dissociates in the stomach to valproic acid. Levels may be raised by aspirin. Can potentiate sedative effects of other medications. Use cautiously with highly protein-bound drugs, since valproic acid can displace them, raising their free fraction. Use cautiously with medications that may cause hepatotoxicity.

continued

Guideline 9: **Safety and Tolerability,** ***continued***

9A. Medications Least Likely to Cause Drug Interactions,[29] *continued*

	Medication	Editors' Comment
Lower second line, more problematic	Fluoxetine	Inhibits many CYP enzymes: substantial inhibition of CYP2D6 and CYP2C9/10, moderate inhibition of CYP2C10, mild inhibition of CYP3A/4. Therefore, may raise levels of many other antidepressants, and of many benzodiazepines, antipsychotics, antiarrhythmics, antihypertensives, and analgesics. Drug interactions persist many weeks after discontinuation due to prolonged half-life of elimination.
	Fluvoxamine	Effects similar to those of fluoxetine except without prolonged half-life.
	Carbamazepine	Induces several CYP enzymes; reduces levels of a variety of other medications.
	Low potency conventional antipsychotics* and tricyclic antidepressants	Both have a wide variety of potential pharmacodynamic interactions and should be used with careful monitoring in patients receiving multiple medications.
	Benzodiazepines	May cause greater sedation, confusion, and ataxia in combination with other medications.

Further Recommendations: ***Do not combine*** monoamine oxidase inhibitors (MAOIs) (including selegiline [Eldepryl] used in Parkinson's disease and Alzheimer's disease) with SSRIs, venlafaxine, buspirone, or tricylic antidepressants. A washout time of 1 to 2 weeks is recommended between stopping MAOIs and beginning these other medications, and 5 weeks or more between stopping fluoxetine and beginning an MAOI.*

[29]Question 29

*Editors' recommendation

Guideline 9:* Safety and Tolerability, *continued

9B. Safest Medications—Least Likely to Cause or Exacerbate Specific Complications[30]

Summary: Sometimes preferred medications for agitation (*Guideline 4*) are problematic for patients with serious comorbid conditions. Table 9B lists potentially effective alternatives for agitation that are less likely to exacerbate comorbid conditions as well as medications that are more likely to cause difficulty.

Likelihood of causing or exacerbating problem: +++ = preferred; unlikely to cause problems ++ = usually not a problem but possible + = more likely – = often

	Antipsychotics				Anxiolytics		Anticonvulsants		Antidepressants		
Complicating Problem	**RSP**	**OLZ**	**HP**	**LP**	**BSP**	**BNZ**	**DVP**	**CBZ**	**SSRIs**	**TCAs**	**TRZ**
Falling due to gait problem other than parkinsonism	++	++	+	–	++	–	++	+	+++	–	+
Very poor memory	++	++	++	–	++	–	++	++	+++	–	++
Nausea or poor appetite	++	++	++	++	++	++	++	+	+	++	++
Lethargy	++	+	+	–	++	–	+	+	++	+	–
Constipation	++	++	++	–	++	++	++	++	+++	–	++
Concern over weight gain	++	+	++	–	++	++	++	++	++	–	++
Prostatic hypertrophy	++	++	++	–	++	++	++	++	+++	–	++
Potential drug abuse or dependence	+++	+++	++	++	++	–	++	++	++	++	++
Congestive heart failure	++*	++*	++	–	++	++	++	++	++	–†	++
Orthostatic hypotension	++*	++*	++	–	++	+	++	++	++	–	–
Cardiac conduction disease	++*	++*	++	–	++	++	++	+	+++	–	+
Angina	++*	++*	++	–	++	++	++	++	++	–†	++
Liver disease—elevated liver function tests	++	++	++	+	++	+	–	–	++	+	++
Renal insufficiency	++	++	++	+	++	++	++	++	++	+	++
Seizure disorder	++	++	++	–	++	++	+++	+++	++	+	++
Chronic obstructive pulmonary disease	++	++	++	+	++	–	++	++	++	++	++
Insomnia‡	+++	+++	++	+++	+	+++	+++	+++	–	+++	+++

RSP: risperidone
OLZ: olanzapine
HP: conventional high potency
LP: conventional low potency
BSP: buspirone
BNZ: benzodiazepines
DVP: divalproex
CBZ: carbamazepine
SSRIs: selective serotonin reuptake inhibitors
TCAs: tricyclic antidepressants
TRZ: trazodone
*Atypical antipsychotics asked about as a class in these conditions
†Nortriptyline low second line in this condition
‡Editors' recommendations
[30]Questions 30–33

Appendix: Mini-Mental State Examination*

Orientation

_____ What is the (year-1) (season-1) (date-1) (day-1) (month-1)? *(5 points possible)*

_____ Where are we: (state-1) (county-1) (city-1) (hospital or clinic-1) (floor-1)? *(5 points possible)*

Registration

Name three objects: 1 second to say each. Ask the patient for all three after you have said them.
_____ Give 1 point for each correct answer. *(3 points)*
Repeat until all three are learned. Count trials and record number _____.

Attention and calculation

_____ Serial sevens backward from 100 (stop after five answers). Alternatively, spell WORLD backward. *(5 points)*

Recall

_____ Ask for the three objects repeated above. One point for each correct answer. *(3 points)*

Language and praxis

_____ Show a pencil and a watch and ask subject to name them. *(2 points)*

_____ Ask the patient to repeat the following: "No ifs, ands, or buts." *(1 point)*

_____ (Three-stage command) "Take this paper in your right hand, fold it in half, and put it on the floor." *(3 points)*

_____ Read and obey the following: "Close your eyes." *(1 point)*

_____ Write a sentence. *(1 point)*

_____ Copy this design (interlocking pentagons). *(1 point)*

_____ **Total score** *(30 points possible)*

(A score of between 25 and 30 on the Mini-Mental State examination is considered normal in older adults; a score between 18 and 24 reflects mild impairment; and a score of less than 18, moderate to severe impairment.)

Please describe most important findings:

*Folstein MF, Folstein SE, McHugh PR. The "Mini-Mental State": a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189–98

Mini-Mental State reproduced with permission from the *Journal of Psychiatric Research*

Suggested Readings

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How to Read the Survey Results

The survey results are given in their entirety on the pages that follow. The components include:

- the question as it was posed to the experts
- the treatment options ordered as they were rated by the experts
- a bar chart depicting the confidence intervals for each of the choices
- a table of numeric values
- a comment by the editors

The 95% Confidence Intervals

We first determined the mean, standard deviation, and 95% confidence interval (CI) for each item. The CI is a statistically calculated range which tells you that, if the survey were repeated with a similar group of experts, there is a 95% chance that the mean score would fall within that range. The 95% CIs for each treatment option are shown as horizontal bars. When the bars do not overlap, it indicates that there is a statistically significant difference between the mean scores of the two choices.

Rating Categories

We designated a rating of first, second, or third line for each item on which there was consensus. This rating was determined by the category into which the 95% CI of its mean score fell. To be rated in the first line category, the entire CI had to fall at or above a score of 6.5 or greater. For an item to be rated second line, the CI had to fall between 3.5 and 6.49. For an item to be rated third line, a portion of the CI had to fall below 3.5. In assigning a rating for each item, we followed a stringent rule to avoid chance upgrading and assigned the lowest rating into which the CI fell. For example, if the bottom of the CI even bordered on the next lower category, we considered the item to be in the lower group.

Note that treatments of choice (items rated "9" by at least half the experts) are indicated by a star. Items on which there was no consensus by a chi-square test of the distribution across the three categories are shown by unshaded CI bars.

Numeric Values

Next to the chart we give a table of numeric values for the mean score (Avg) and standard deviation (SD) for each item, and the percentage of experts who rated the option first, second, and third line, as well as treatment of choice. (Note: the percentage for treatment of choice is also included in the total percentage for first line.)

Comment

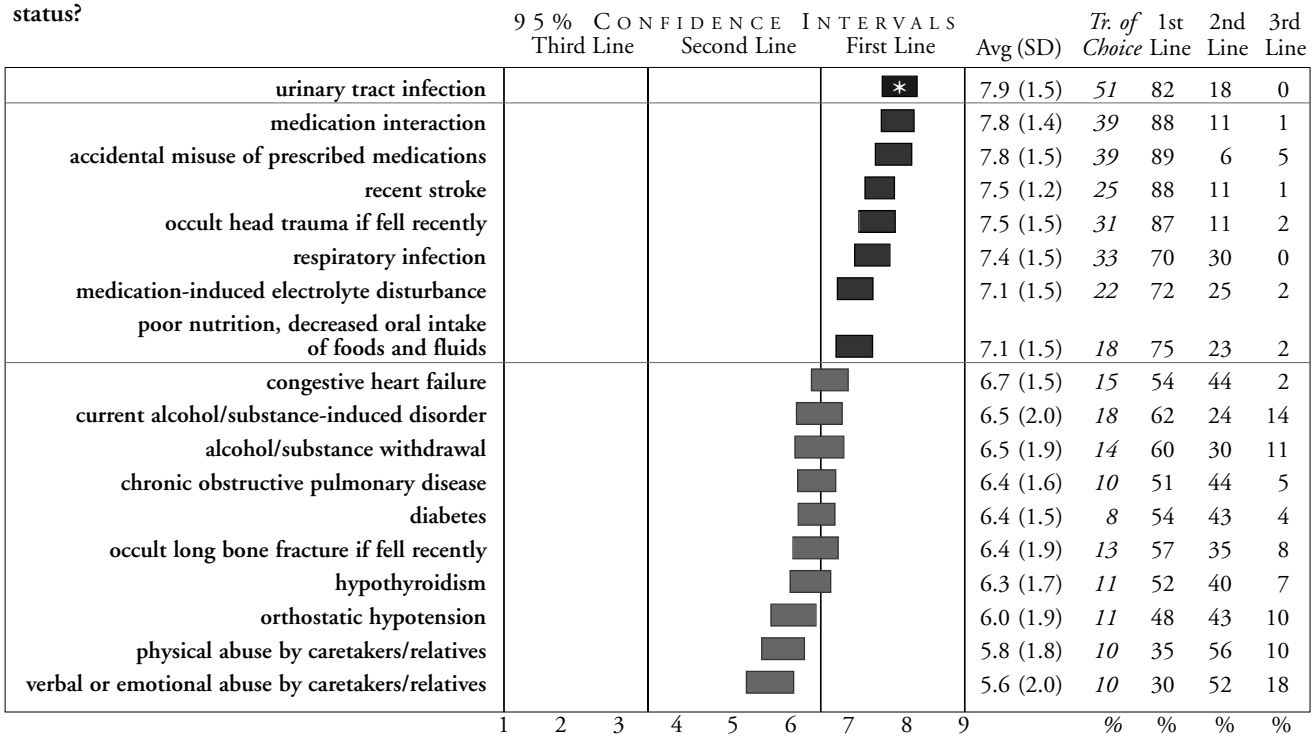
The comment explains how the results relate to the recommendations presented in the Guidelines.

How to Read the Figure

Look at the section of the graphic for Survey Question 6 that presents the ratings for the long-term treatment of an agitated patient with dementia who has prominent psychotic symptoms (p. 51). The placement of the boxes shows that the experts rated risperidone and conventional high potency antipsychotics as first line options. The bar for olanzapine straddles the boundary between the first and second line categories, resulting in a top-tier second line rating. The boxes for these three options overlap, indicating that the ratings for these treatments are not statistically significantly different. Other highly rated second line options are divalproex and trazodone. Note that the boxes for divalproex and carbamazepine do not overlap, indicating that there is a statistically significant difference in the ratings for these two choices. The box for benzodiazepines falls entirely in the third line category.

1 In your INITIAL EVALUATION of an agitated patient with dementia in the office or nursing home, which of the following are most important to focus on as possible causes of recently altered mental status?

Comment: The experts recommend an exhaustive differential diagnosis to pursue the underlying cause of a change in mental status, with particular attention to urinary tract infections, drug interactions, accidental misuse of prescribed medications, a recent stroke, an occult head injury from a recent fall, respiratory infection, medication-induced electrolyte disturbances, and poor oral intake of foods and/or fluids.

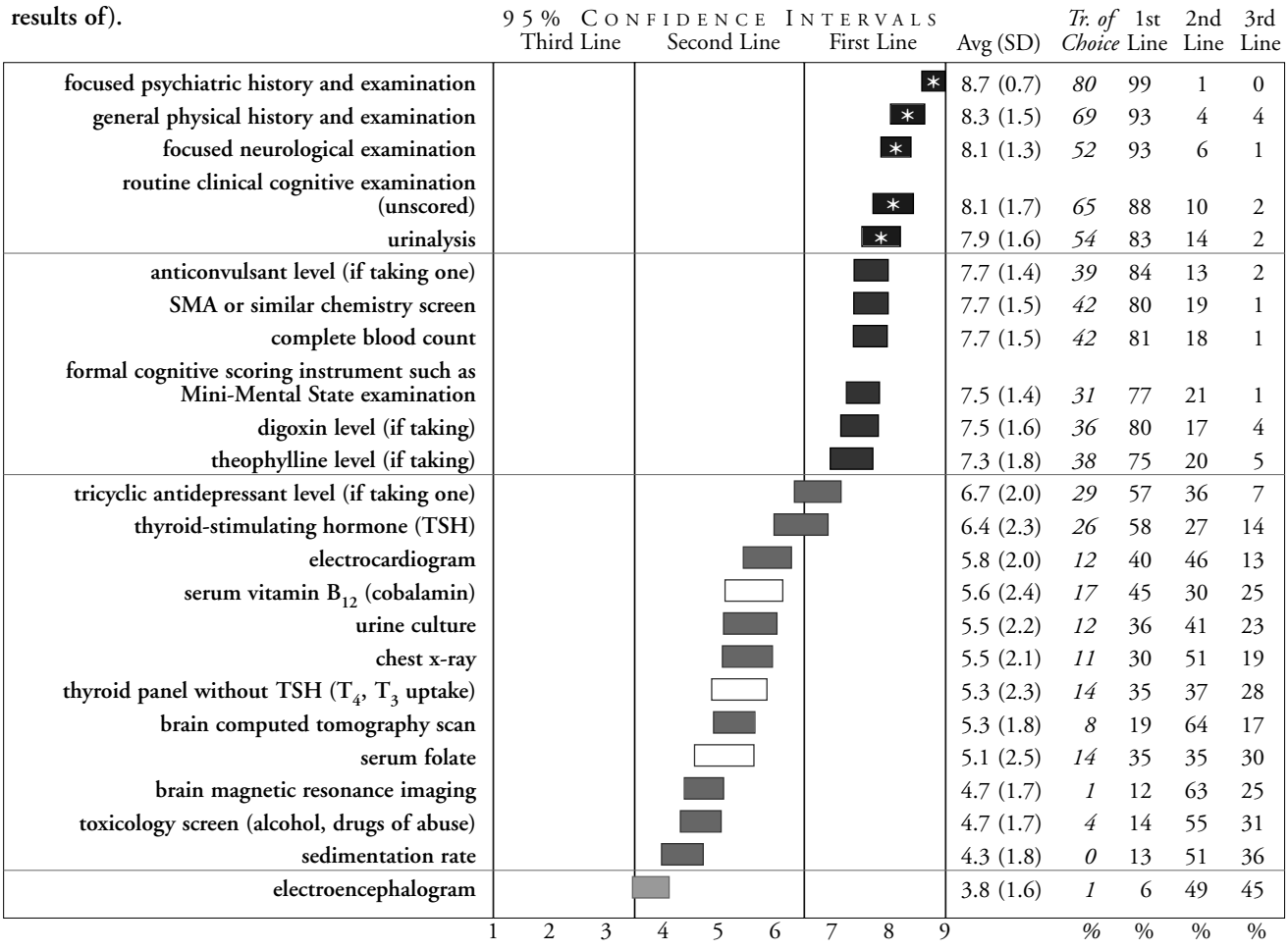


	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
urinary tract infection	7.9 (1.5)	*51*	82	18	0
medication interaction	7.8 (1.4)	*39*	88	11	1
accidental misuse of prescribed medications	7.8 (1.5)	*39*	89	6	5
recent stroke	7.5 (1.2)	*25*	88	11	1
occult head trauma if fell recently	7.5 (1.5)	*31*	87	11	2
respiratory infection	7.4 (1.5)	*33*	70	30	0
medication-induced electrolyte disturbance	7.1 (1.5)	*22*	72	25	2
poor nutrition, decreased oral intake of foods and fluids	7.1 (1.5)	*18*	75	23	2
congestive heart failure	6.7 (1.5)	*15*	54	44	2
current alcohol/substance-induced disorder	6.5 (2.0)	*18*	62	24	14
alcohol/substance withdrawal	6.5 (1.9)	*14*	60	30	11
chronic obstructive pulmonary disease	6.4 (1.6)	*10*	51	44	5
diabetes	6.4 (1.5)	*8*	54	43	4
occult long bone fracture if fell recently	6.4 (1.9)	*13*	57	35	8
hypothyroidism	6.3 (1.7)	*11*	52	40	7
orthostatic hypotension	6.0 (1.9)	*11*	48	43	10
physical abuse by caretakers/relatives	5.8 (1.8)	*10*	35	56	10
verbal or emotional abuse by caretakers/relatives	5.6 (2.0)	*10*	30	52	18
		%	%	%	%

* = *Treatment of Choice* ☐ = *No Consensus* *Note: 1st Line percentage includes Treatment of Choice percentage*

2 ASSESSMENT: Suppose you are seeing a new patient in your office or a nursing home. The patient has had dementia for some time, but in recent weeks has developed a subacute change in mental status characterized by increased confusion and agitation. Please rate each of the following assessments as tests you would now perform (or need to see very recent results of).

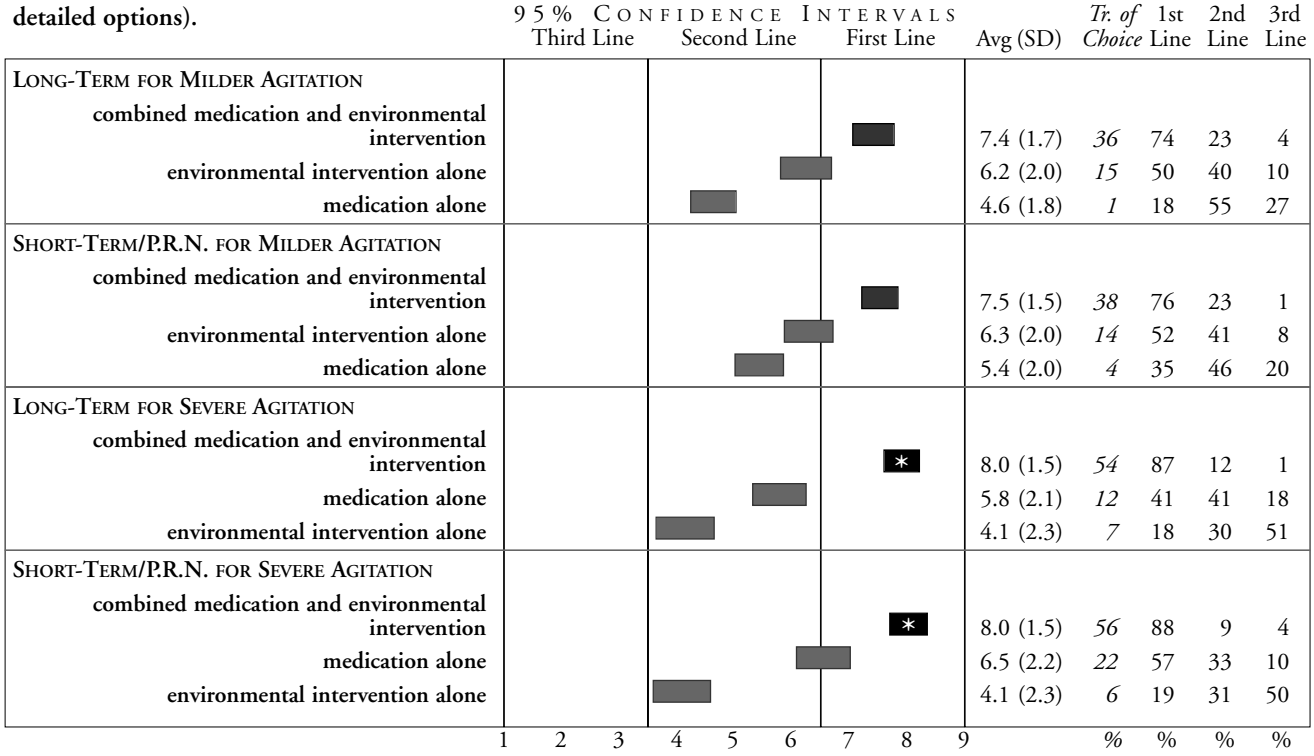
Comment: There are many assessments and tests from which to choose in evaluating a change in mental status. We asked the experts to prioritize a list of common assessments. The options that were rated first line are those the experts recommend performing, or at least considering, as part of the routine evaluation of most patients. The results of these initial assessments can then guide the clinician's selection of additional tests that are more focused, specific, and often expensive. Note that some assessments provide positive guidance in identifying the etiology of the change in the patient's status (e.g., urinalysis, urine culture), while others provide negative guidance (e.g., the absence of drug toxicity suggesting that the clinician should focus on other causes of mental status change such as respiratory disease or stroke).



* = Treatment of Choice = No Consensus Note: 1st Line percentage includes Treatment of Choice percentage

3 General Treatment Planning: Please rate each of the following overall approaches to treating agitation in an elderly patient with dementia. Give ratings in the 7–9 range for the approaches you use most often in your own practice and lower ratings to approaches you use less often. By "environmental intervention," we mean a wide range of psychosocial and behavioral treatments, i.e., anything that is not a medication (see Survey Question 4 for detailed options).

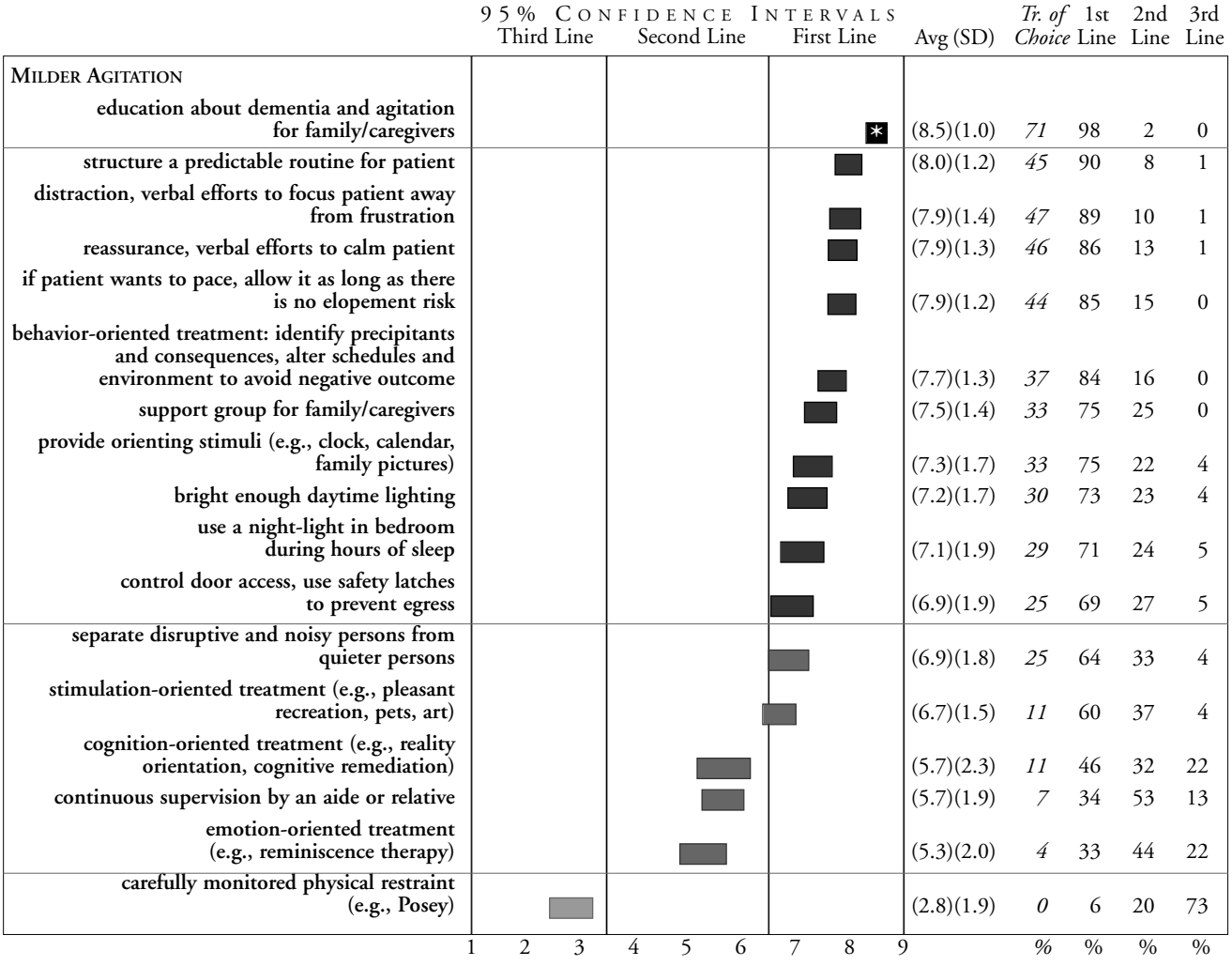
Comment: The experts emphatically recommend that the treatment for agitated dementia combine both medication and environmental intervention in almost all situations, regardless of the severity of the presentation or the length of treatment. This recommendation is especially important because there is often a tendency to neglect environmental interventions in formulating a treatment plan for such patients. For patients with mild agitation, the experts consider environmental intervention alone as sometimes sufficient. However, in severe agitation, medication alone is sometimes appropriate, for example, if the patient is in danger or the environment cannot be changed.



* = Treatment of Choice = No Consensus *Note: 1st Line percentage includes Treatment of Choice percentage*

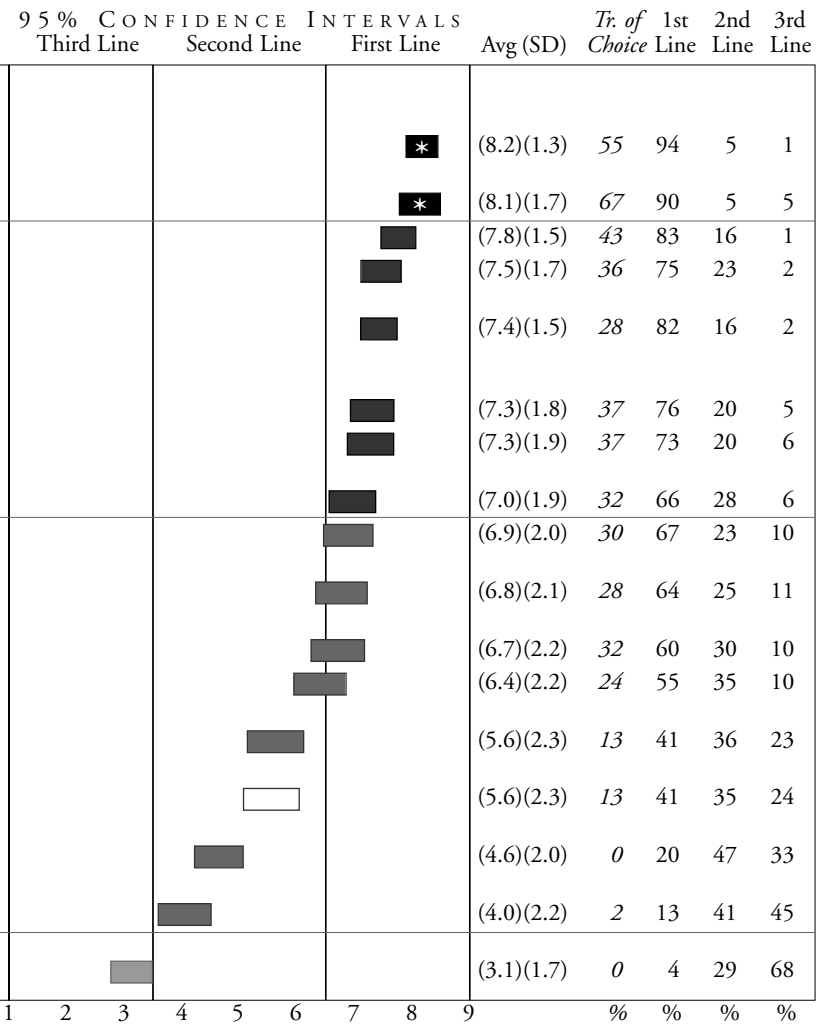
4 SPECIFIC CHOICE OF ENVIRONMENTAL INTERVENTION. Assume that at some point you wish to use environmental interventions (with or without medication). Please rate the appropriateness of each of the following interventions.

Comment: The experts selected many types of environmental intervention. Education for family and caregivers is essential for both mild and more severe agitation. Under the burden of care, families and caregivers often develop depression, anxiety, or irritability that may interfere with the patient's care. Clarifying the expectations for patient care and assisting caregivers to make arrangements for help and respite may have a significant impact on the patient's care. Otherwise, the particular type of environmental intervention to select varies somewhat depending on the severity of the agitation. Control and supervision are more often necessary for patients with severe agitation, whereas distraction, reassurance, and orienting stimuli may be most effective for patients with mild agitation. Physical restraints are generally to be avoided in mild agitation and used only with caution in severe agitation.



* = *Treatment of Choice* □ = *No Consensus* *Note: 1st Line percentage includes Treatment of Choice percentage*

4 *continued*

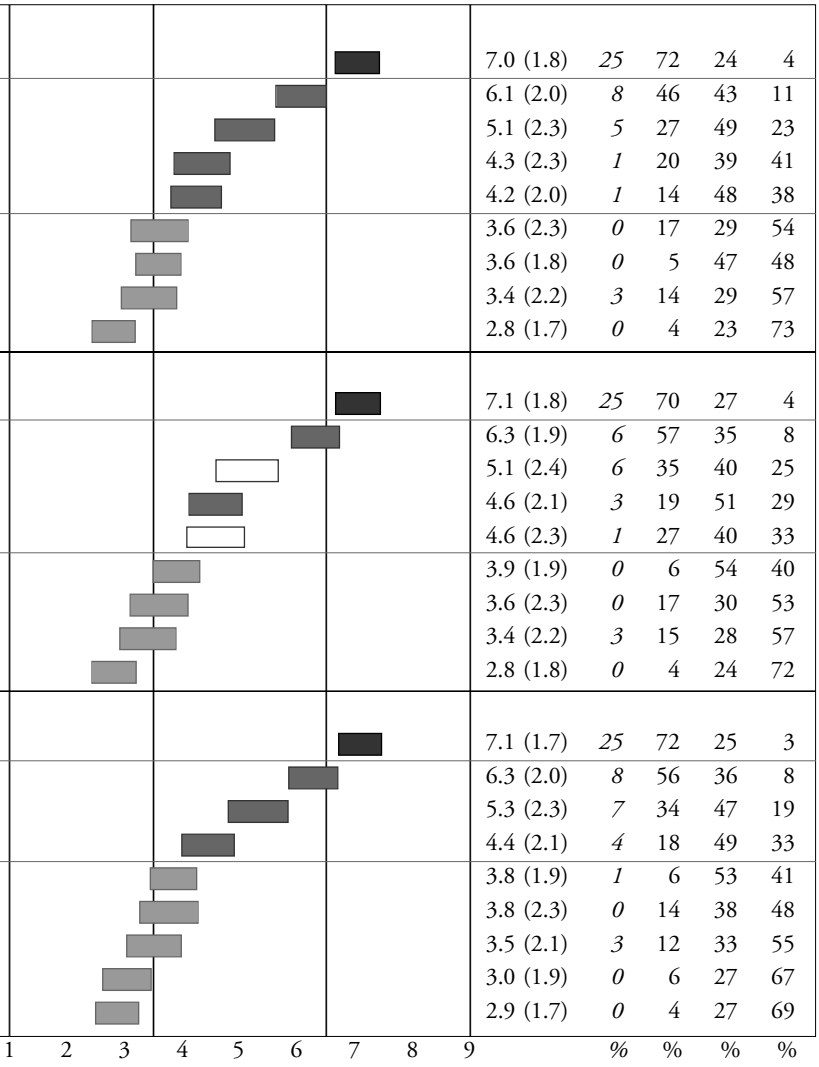


	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
Severe Agitation					
control door access, use safety latches to prevent egress	(8.2)(1.3)	*55*	94	5	1
education about dementia and agitation for family/caregivers	(8.1)(1.7)	*67*	90	5	5
continuous supervision by an aide or relative	(7.8)(1.5)	*43*	83	16	1
support group for family/caregivers	(7.5)(1.7)	*36*	75	23	2
separate disruptive and noisy persons from quieter persons	(7.4)(1.5)	*28*	82	16	2
behavior-oriented treatment: identify precipitants and consequences, alter schedules and environment to avoid negative outcome	(7.3)(1.8)	*37*	76	20	5
structure a predictable routine for patient	(7.3)(1.9)	*37*	73	20	6
distraction, verbal efforts to focus patient away from frustration	(7.0)(1.9)	*32*	66	28	6
bright enough daytime lighting	(6.9)(2.0)	*30*	67	23	10
use a night-light in bedroom during hours of sleep	(6.8)(2.1)	*28*	64	25	11
if patient wants to pace, allow it as long as there is no elopement risk	(6.7)(2.2)	*32*	60	30	10
reassurance, verbal efforts to calm patient	(6.4)(2.2)	*24*	55	35	10
carefully monitored physical restraint (e.g., Posey)	(5.6)(2.3)	*13*	41	36	23
provide orienting stimuli (e.g., clock, calendar, family pictures)	(5.6)(2.3)	*13*	41	35	24
stimulation-oriented treatment (e.g., pleasant recreation, pets, art)	(4.6)(2.0)	*0*	20	47	33
cognition-oriented treatment (e.g., reality orientation, cognitive remediation)	(4.0)(2.2)	*2*	13	41	45
emotion-oriented treatment (e.g., reminiscence therapy)	(3.1)(1.7)	*0*	4	29	68
		%	%	%	%

* = *Treatment of Choice* ☐ = *No Consensus* *Note: 1st Line percentage includes Treatment of Choice percentage*

5 Suppose a patient with previously stable dementia experiences several weeks of increasing confusion and agitation due to DELIRIUM brought on by one of the medical conditions shown below. Assume the medical condition is receiving proper treatment, but that the agitation warrants an additional medication. Please rate each of the following medications for agitation in each situation on the basis of both safety and efficacy.

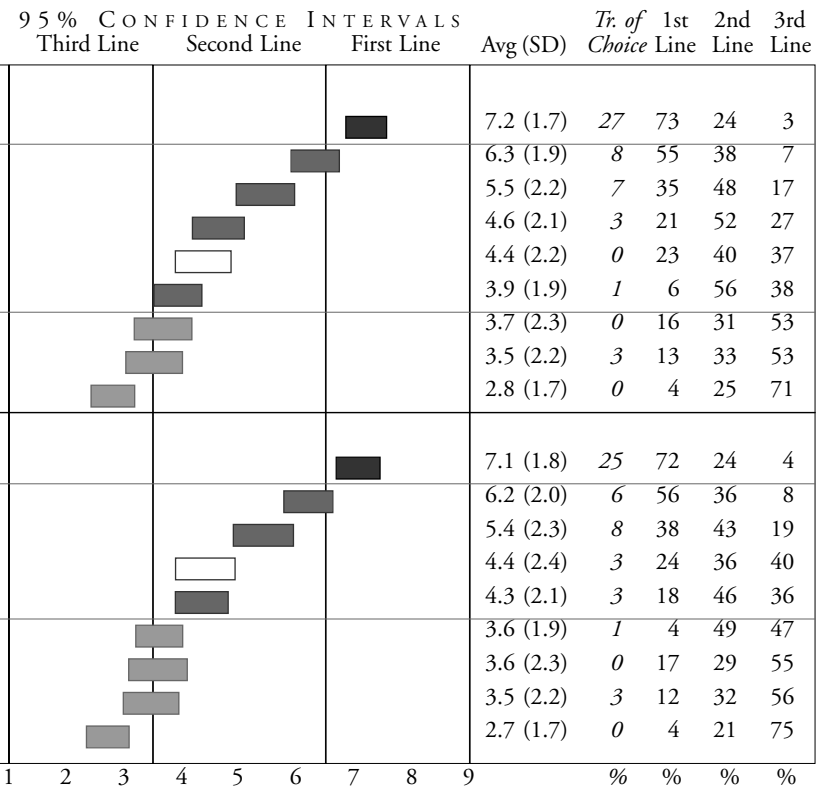
Comment: Patients with dementia may develop a superimposed delirium that is brought on by a medical condition (e.g., congestive heart failure, upper respiratory infection [URI], urinary tract infection [UTI], chronic obstructive pulmonary disease [COPD]). Although the causes of delirium require emergency medical treatment, delirium-induced agitation may also require symptomatic treatment while the underlying medical condition is being treated. For treatment of delirium-induced agitation, the experts prefer an agent that will act relatively quickly and cause few drug interactions. Their first line choice is a conventional high potency antipsychotic, perhaps because these medications can be administered by injection. Risperidone is the top second line choice. The experts do not favor the use of benzodiazepines in delirium, perhaps because these medications may increase disorientation.



	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
CONGESTIVE HEART FAILURE					
conventional high potency antipsychotic	7.0 (1.8)	*25*	72	24	4
risperidone	6.1 (2.0)	*8*	46	43	11
olanzapine	5.1 (2.3)	*5*	27	49	23
benzodiazepine	4.3 (2.3)	*1*	20	39	41
trazodone	4.2 (2.0)	*1*	14	48	38
buspirone	3.6 (2.3)	*0*	17	29	54
conventional low potency antipsychotic	3.6 (1.8)	*0*	5	47	48
divalproex	3.4 (2.2)	*3*	14	29	57
carbamazepine	2.8 (1.7)	*0*	4	23	73
INFECTION (URI, UTI)					
conventional high potency antipsychotic	7.1 (1.8)	*25*	70	27	4
risperidone	6.3 (1.9)	*6*	57	35	8
olanzapine	5.1 (2.4)	*6*	35	40	25
trazodone	4.6 (2.1)	*3*	19	51	29
benzodiazepine	4.6 (2.3)	*1*	27	40	33
conventional low potency antipsychotic	3.9 (1.9)	*0*	6	54	40
buspirone	3.6 (2.3)	*0*	17	30	53
divalproex	3.4 (2.2)	*3*	15	28	57
carbamazepine	2.8 (1.8)	*0*	4	24	72
COPD OR PNEUMONIA					
conventional high potency antipsychotic	7.1 (1.7)	*25*	72	25	3
risperidone	6.3 (2.0)	*8*	56	36	8
olanzapine	5.3 (2.3)	*7*	34	47	19
trazodone	4.4 (2.1)	*4*	18	49	33
conventional low potency antipsychotic	3.8 (1.9)	*1*	6	53	41
buspirone	3.8 (2.3)	*0*	14	38	48
divalproex	3.5 (2.1)	*3*	12	33	55
benzodiazepine	3.0 (1.9)	*0*	6	27	67
carbamazepine	2.9 (1.7)	*0*	4	27	69
			%	%	%	%

* = *Treatment of Choice* ☐ = *No Consensus* *Note: 1st Line percentage includes Treatment of Choice percentage*

5 *continued*



	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
Diabetes					
conventional high potency antipsychotic	7.2 (1.7)	*27*	73	24	3
risperidone	6.3 (1.9)	*8*	55	38	7
olanzapine	5.5 (2.2)	*7*	35	48	17
trazodone	4.6 (2.1)	*3*	21	52	27
benzodiazepine	4.4 (2.2)	*0*	23	40	37
conventional low potency antipsychotic	3.9 (1.9)	*1*	6	56	38
buspirone	3.7 (2.3)	*0*	16	31	53
divalproex	3.5 (2.2)	*3*	13	33	53
carbamazepine	2.8 (1.7)	*0*	4	25	71
Dehydration or Electrolyte Imbalance					
conventional high potency antipsychotic	7.1 (1.8)	*25*	72	24	4
risperidone	6.2 (2.0)	*6*	56	36	8
olanzapine	5.4 (2.3)	*8*	38	43	19
benzodiazepine	4.4 (2.4)	*3*	24	36	40
trazodone	4.3 (2.1)	*3*	18	46	36
conventional low potency antipsychotic	3.6 (1.9)	*1*	4	49	47
buspirone	3.6 (2.3)	*0*	17	29	55
divalproex	3.5 (2.2)	*3*	12	32	56
carbamazepine	2.7 (1.7)	*0*	4	21	75
		%	%	%	%

* = *Treatment of Choice* ☐ = *No Consensus* *Note: 1st Line percentage includes Treatment of Choice percentage*

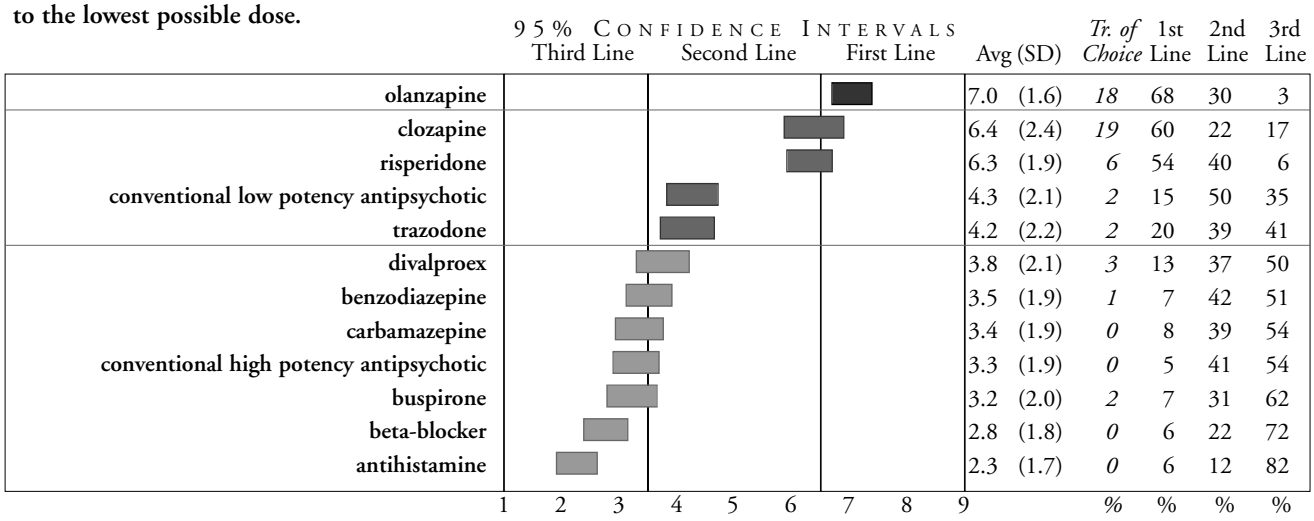
6 Please rate each of the following for a patient with severe agitation dominated by prominent PSYCHOTIC SYMPTOMS, including actions resulting from delusions or hallucinations. Please rate each item separately for both short-term/p.r.n. and long-term use.

Comment: For longer-term management of psychotic symptoms accompanying dementia and agitation, the experts recommend risperidone followed by a conventional antipsychotic as first line options. Olanzapine is a highly rated second line option. Atypical antipsychotics have a lower risk than conventional antipsychotics of causing extrapyramidal symptoms in long-term treatment of most patients with dementia. Divalproex and trazodone are options to consider if an antipsychotic is not effective. For very short-term treatment, the experts' first line choice is a conventional high potency antipsychotic (e.g., haloperidol), with risperidone a highly rated second line alternative. This ordering may reflect the availability of conventional antipsychotics for parenteral administration. It should be noted that this expert survey was done before quetiapine and other newer atypical antipsychotics were available.

	95% CONFIDENCE INTERVALS Third Line / Second Line / First Line	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
LONG-TERM						
risperidone		7.3 (1.6)	*24*	77	17	6
conventional high potency antipsychotic		6.9 (1.7)	*22*	67	28	5
olanzapine		6.6 (1.9)	*18*	59	33	8
divalproex		5.7 (1.9)	*9*	38	48	14
trazodone		5.1 (2.0)	*2*	25	53	22
carbamazepine		4.5 (2.1)	*4*	21	45	34
clozapine		4.3 (2.0)	*2*	12	53	35
conventional low potency antipsychotic		4.0 (2.1)	*1*	16	41	43
benzodiazepine		2.6 (1.4)	*0*	2	20	78
SHORT-TERM/P.R.N.						
conventional high potency antipsychotic		7.5 (1.5)	*35*	78	21	1
risperidone		6.5 (2.2)	*14*	62	27	11
olanzapine		5.8 (2.4)	*13*	47	35	19
benzodiazepine		5.0 (2.1)	*4*	29	38	33
trazodone		4.9 (2.2)	*4*	23	49	28
conventional low potency antipsychotic		4.1 (2.3)	*1*	14	46	40
divalproex		3.9 (2.2)	*3*	13	42	46
carbamazepine		3.0 (1.9)	*0*	7	24	68
clozapine		2.9 (2.0)	*1*	6	27	67
	1 2 3 4 5 6 7 8 9		*%*	%	%	%

7 Please rate each of the following for ongoing use in a patient who has PARKINSON'S DISEASE WITH AGITATION AND PSYCHOSIS specifically due to the use of L-dopa, carbidopa-levodopa (Sinemet), or another dopamine agonist. Assume you have lowered the dopaminergic medication to the lowest possible dose.

Comment: To treat a patient with Parkinson's disease who has agitation and psychosis due specifically to the use of L-dopa, Sinemet, or another dopamine agonist, the experts clearly prefer the atypical antipsychotics, probably because they have a lower risk of extrapyramidal side effects that might exacerbate the parkinsonism. The editors note that, in this question and in every other question where we asked about an antihistamine, the experts gave this option a uniformly low rating, probably because of the propensity of this class of medication to cause cognitive impairment and oversedation.

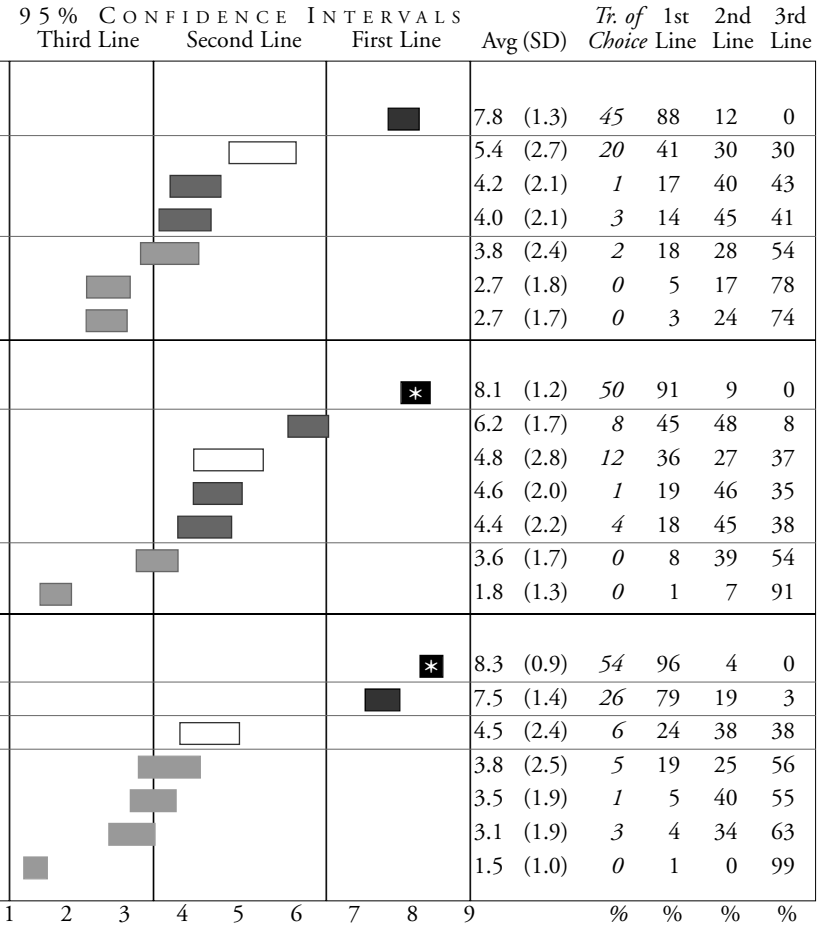


	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
olanzapine	7.0 (1.6)	*18*	68	30	3
clozapine	6.4 (2.4)	*19*	60	22	17
risperidone	6.3 (1.9)	*6*	54	40	6
conventional low potency antipsychotic	4.3 (2.1)	*2*	15	50	35
trazodone	4.2 (2.2)	*2*	20	39	41
divalproex	3.8 (2.1)	*3*	13	37	50
benzodiazepine	3.5 (1.9)	*1*	7	42	51
carbamazepine	3.4 (1.9)	*0*	8	39	54
conventional high potency antipsychotic	3.3 (1.9)	*0*	5	41	54
buspirone	3.2 (2.0)	*2*	7	31	62
beta-blocker	2.8 (1.8)	*0*	6	22	72
antihistamine	2.3 (1.7)	*0*	6	12	82
		%	%	%	%

* = *Treatment of Choice* = *No Consensus* *Note: 1st Line percentage includes Treatment of Choice percentage*

8 Please rate each of the following overall strategies for treating prominent DEPRESSIVE SYMPTOMS in an elderly patient with dementia and agitation. (In Survey Question 24, you will be able to specify your choice of antidepressants.) Please note that the severity ranges refer to *depression* rather than agitation.

Comment: For mild to moderate depression, the experts' first line choice is an antidepressant alone. For severe depression, the experts rate an antidepressant alone as treatment of choice and electroconvulsive therapy (ECT) as the top second line option. For psychotic depression, the combination of an antidepressant and an antipsychotic is rated as the treatment of choice, with ECT a first line alternative. Many geriatric patients with dementia fail to respond to or may be unable to tolerate the combination of an antidepressant and antipsychotic and therefore may need ECT. The experts do not recommend psychotherapy alone, regardless of the severity of the depression. Many of the experts suggest that a combination approach may be helpful, especially for milder depression, although there was no consensus on this option.

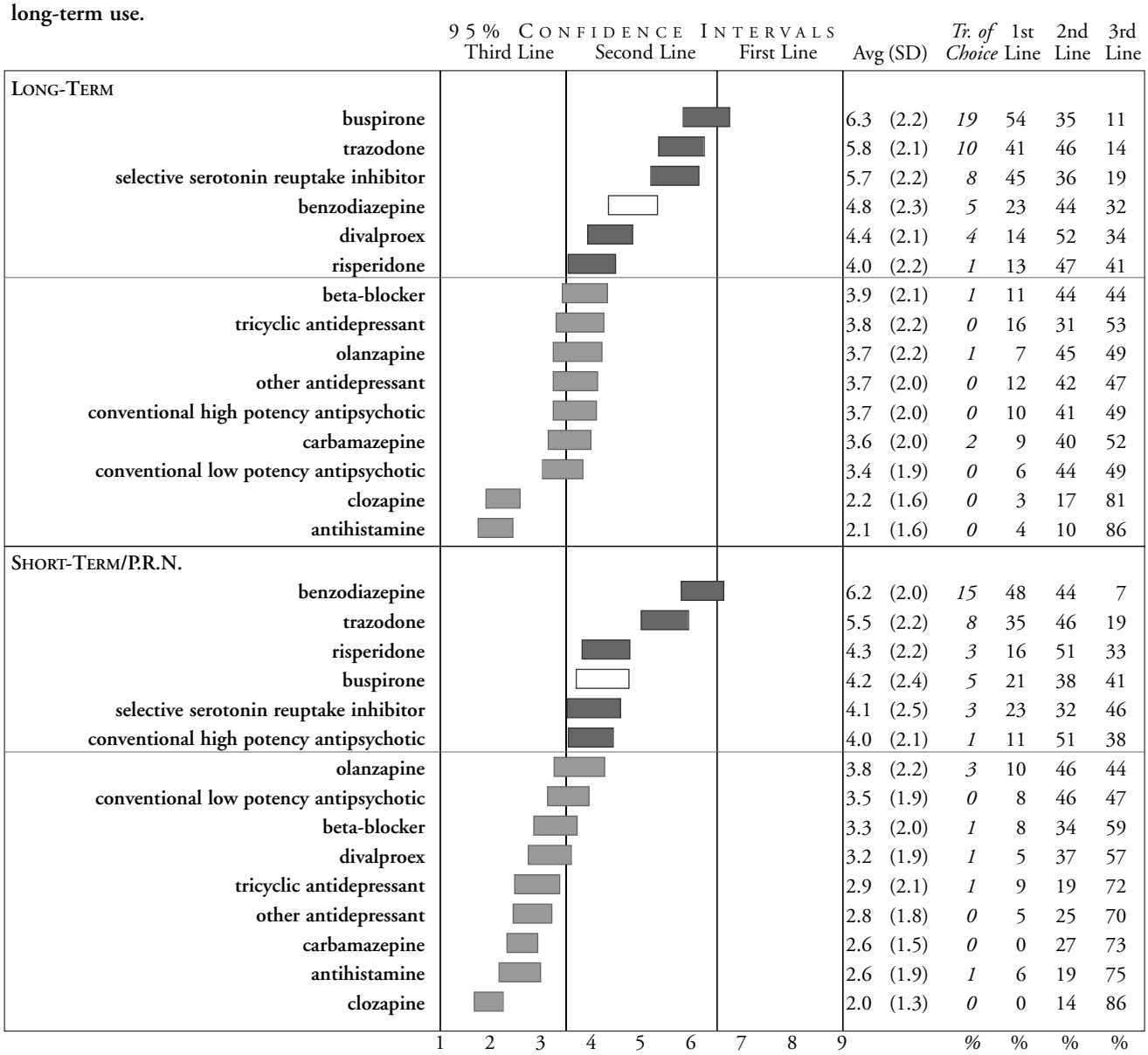


	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
MILD TO MODERATE DEPRESSION					
antidepressant alone	7.8 (1.3)	*45*	88	12	0
psychotherapy plus meds as you chose above	5.4 (2.7)	*20*	41	30	30
antidepressant plus benzodiazepine	4.2 (2.1)	*1*	17	40	43
antidepressant plus buspirone	4.0 (2.1)	*3*	14	45	41
specific psychotherapy for depression, no meds	3.8 (2.4)	*2*	18	28	54
antidepressant plus antipsychotic	2.7 (1.8)	*0*	5	17	78
electroconvulsive therapy	2.7 (1.7)	*0*	3	24	74
SEVERE DEPRESSION, NO PSYCHOSIS					
antidepressant alone	8.1 (1.2)	*50*	91	9	0
electroconvulsive therapy	6.2 (1.7)	*8*	45	48	8
psychotherapy plus meds as you chose above	4.8 (2.8)	*12*	36	27	37
antidepressant plus benzodiazepine	4.6 (2.0)	*1*	19	46	35
antidepressant plus buspirone	4.4 (2.2)	*4*	18	45	38
antidepressant plus antipsychotic	3.6 (1.7)	*0*	8	39	54
specific psychotherapy for depression, no meds	1.8 (1.3)	*0*	1	7	91
SEVERE DEPRESSION WITH PSYCHOSIS					
antidepressant plus antipsychotic	8.3 (0.9)	*54*	96	4	0
electroconvulsive therapy	7.5 (1.4)	*26*	79	19	3
antidepressant alone	4.5 (2.4)	*6*	24	38	38
psychotherapy plus meds as you chose above	3.8 (2.5)	*5*	19	25	56
antidepressant plus benzodiazepine	3.5 (1.9)	*1*	5	40	55
antidepressant plus buspirone	3.1 (1.9)	*3*	4	34	63
specific psychotherapy for depression, no meds	1.5 (1.0)	*0*	1	0	99
		%	%	%	%

* = *Treatment of Choice* ☐ = *No Consensus* *Note: 1st Line percentage includes Treatment of Choice percentage*

9 Please rate each of the following medications for an elderly patient with dementia and moderate agitation characterized by prominent GENERALIZED ANXIETY SYMPTOMS. Please rate each medication separately for both short-term/p.r.n. and long-term use.

Comment: The experts do not have a clear first line recommendation for patients with prominent generalized anxiety symptoms. For long-term treatment, buspirone is the top-rated option, followed by trazodone and the selective serotonin reuptake inhibitors (SSRIs). Buspirone and SSRIs usually have gradual onsets of action. Benzodiazepines and trazodone, which act rapidly, are preferred for short-term treatment. However, benzodiazepines receive low ratings for long-term treatment, probably because of their side effects on memory, orientation, and paradoxical agitation.



	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
LONG-TERM					
buspirone	6.3 (2.2)	*19*	54	35	11
trazodone	5.8 (2.1)	*10*	41	46	14
selective serotonin reuptake inhibitor	5.7 (2.2)	*8*	45	36	19
benzodiazepine	4.8 (2.3)	*5*	23	44	32
divalproex	4.4 (2.1)	*4*	14	52	34
risperidone	4.0 (2.2)	*1*	13	47	41
beta-blocker	3.9 (2.1)	*1*	11	44	44
tricyclic antidepressant	3.8 (2.2)	*0*	16	31	53
olanzapine	3.7 (2.2)	*1*	7	45	49
other antidepressant	3.7 (2.0)	*0*	12	42	47
conventional high potency antipsychotic	3.7 (2.0)	*0*	10	41	49
carbamazepine	3.6 (2.0)	*2*	9	40	52
conventional low potency antipsychotic	3.4 (1.9)	*0*	6	44	49
clozapine	2.2 (1.6)	*0*	3	17	81
antihistamine	2.1 (1.6)	*0*	4	10	86
SHORT-TERM/P.R.N.					
benzodiazepine	6.2 (2.0)	*15*	48	44	7
trazodone	5.5 (2.2)	*8*	35	46	19
risperidone	4.3 (2.2)	*3*	16	51	33
buspirone	4.2 (2.4)	*5*	21	38	41
selective serotonin reuptake inhibitor	4.1 (2.5)	*3*	23	32	46
conventional high potency antipsychotic	4.0 (2.1)	*1*	11	51	38
olanzapine	3.8 (2.2)	*3*	10	46	44
conventional low potency antipsychotic	3.5 (1.9)	*0*	8	46	47
beta-blocker	3.3 (2.0)	*1*	8	34	59
divalproex	3.2 (1.9)	*1*	5	37	57
tricyclic antidepressant	2.9 (2.1)	*1*	9	19	72
other antidepressant	2.8 (1.8)	*0*	5	25	70
carbamazepine	2.6 (1.5)	*0*	0	27	73
antihistamine	2.6 (1.9)	*1*	6	19	75
clozapine	2.0 (1.3)	*0*	0	14	86
		%	%	%	%

* = *Treatment of Choice* ☐ = *No Consensus* *Note: 1st Line percentage includes Treatment of Choice percentage*

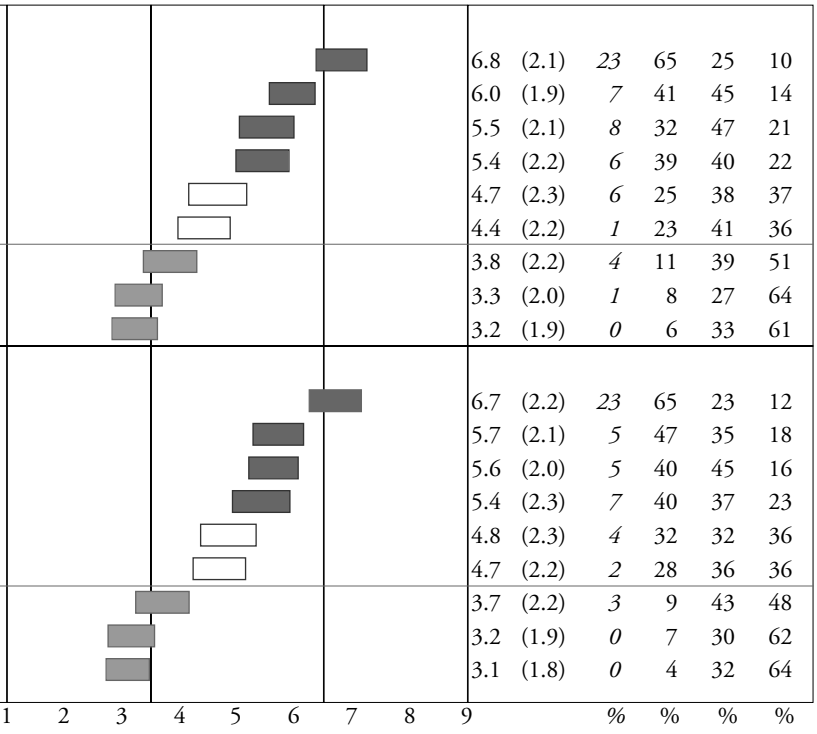
10 Please rate each of the following medications for an elderly patient with dementia who has prominent INSOMNIA WITHOUT MARKEDLY WORSE CONFUSION OR AGITATION AT NIGHT (i.e., not a "sundowner"). Please rate each medication separately for both short-term/p.r.n. and long-term use.

Comment: The experts' first line choice for the long- and short-term treatment of patients with prominent insomnia who are not sundowners is trazodone. Trazodone is nonaddicting and is less likely to exacerbate memory loss or disorientation than are benzodiazepines. Although the experts consider benzodiazepines a second line option for short-term treatment, they recommend avoiding the long-term use of benzodiazepines in this patient population. Benzodiazepines may exacerbate confusion and are associated with increased memory deficits, falls, addiction, and withdrawal symptoms. If trazodone is ineffective, the experts have no clear recommendation for the next choice, but the medication should be selected on the basis of the side effect profile that is likely to be best for the individual patient.

	95% CONFIDENCE INTERVALS Third Line / Second Line / First Line	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
LONG-TERM						
trazodone		7.4 (1.8)	*31*	80	17	4
benzodiazepine		4.0 (2.5)	*5*	17	33	51
tricyclic antidepressant		3.6 (2.2)	*1*	12	33	55
olanzapine		3.4 (1.8)	*0*	8	37	55
conventional low potency antipsychotic		3.4 (1.9)	*0*	7	35	58
risperidone		3.3 (1.8)	*0*	6	37	57
divalproex		3.2 (2.1)	*1*	10	28	62
conventional high potency antipsychotic		3.2 (1.8)	*0*	7	30	63
carbamazepine		2.6 (1.7)	*0*	4	23	74
SHORT-TERM/P.R.N.						
trazodone		7.3 (1.8)	*34*	78	18	4
benzodiazepine		5.7 (2.3)	*10*	43	37	19
tricyclic antidepressant		3.7 (2.2)	*1*	12	33	55
conventional low potency antipsychotic		3.7 (2.0)	*1*	8	40	52
olanzapine		3.6 (1.8)	*0*	7	45	49
conventional high potency antipsychotic		3.4 (1.7)	*0*	6	40	54
risperidone		3.4 (1.7)	*0*	4	45	52
divalproex		3.0 (1.9)	*1*	5	25	70
carbamazepine		2.5 (1.5)	*0*	2	19	78
	1 2 3 4 5 6 7 8 9		*%*	%	%	%

11 Please rate each of the following medications for an elderly patient with dementia who has prominent INSOMNIA, DISORIENTATION, AND AGITATION AT NIGHT, but who is relatively calm during the day (i.e., "sundowning"). Please rate each medication separately for both short-term/p.r.n. and long-term use.

Comment: Trazodone is preferred among the possible options for the sundowning patient, probably because of its short half-life and its sedating properties. The experts recommend avoiding the long-term use of benzodiazepines in this population for the reasons mentioned in the comment on Survey Question 10.

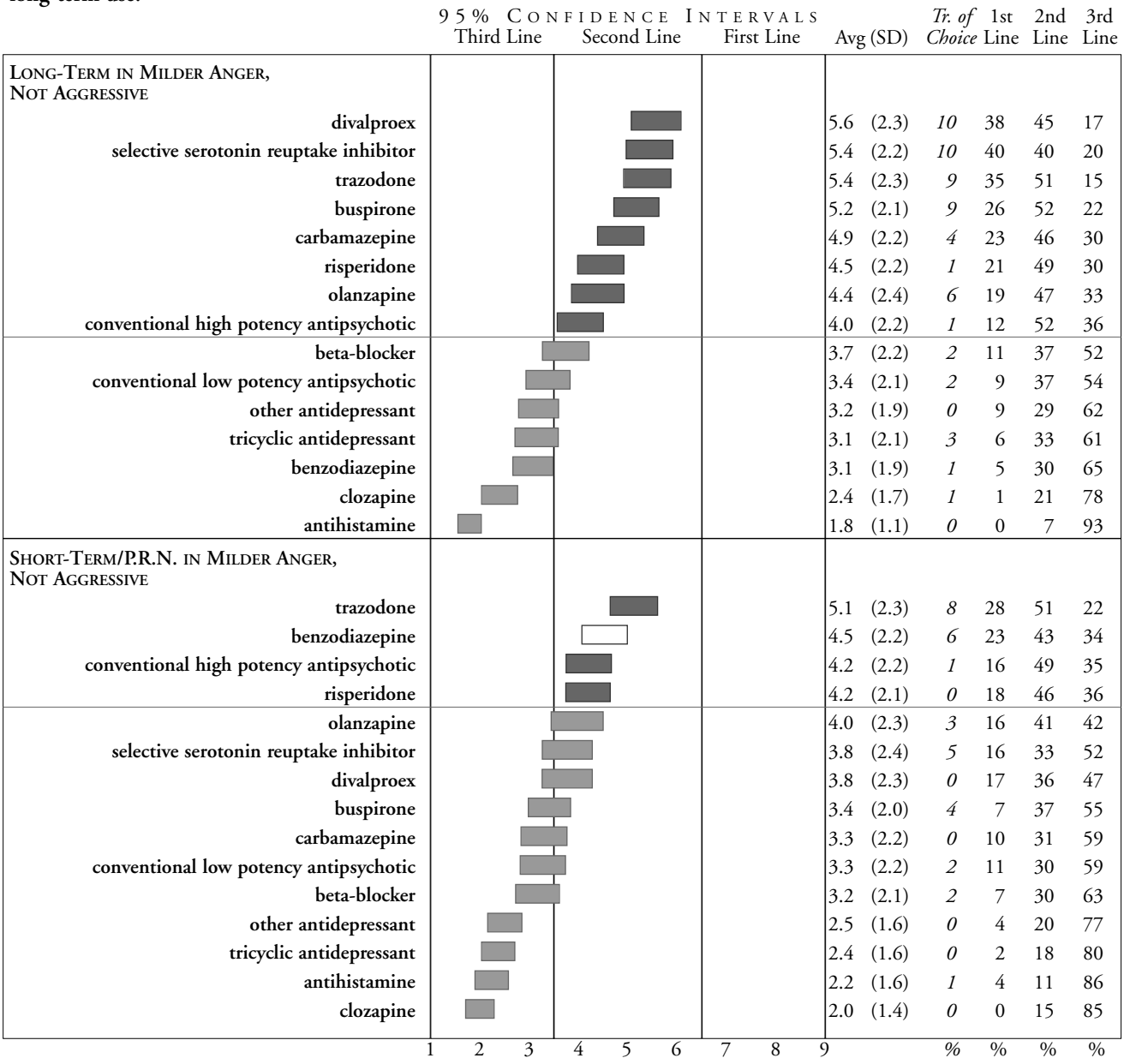


	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
LONG-TERM					
trazodone	6.8 (2.1)	*23*	65	25	10
risperidone	6.0 (1.9)	*7*	41	45	14
olanzapine	5.5 (2.1)	*8*	32	47	21
conventional high potency antipsychotic	5.4 (2.2)	*6*	39	40	22
divalproex	4.7 (2.3)	*6*	25	38	37
conventional low potency antipsychotic	4.4 (2.2)	*1*	23	41	36
carbamazepine	3.8 (2.2)	*4*	11	39	51
benzodiazepine	3.3 (2.0)	*1*	8	27	64
tricyclic antidepressant	3.2 (1.9)	*0*	6	33	61
SHORT-TERM/P.R.N.					
trazodone	6.7 (2.2)	*23*	65	23	12
conventional high potency antipsychotic	5.7 (2.1)	*5*	47	35	18
risperidone	5.6 (2.0)	*5*	40	45	16
olanzapine	5.4 (2.3)	*7*	40	37	23
benzodiazepine	4.8 (2.3)	*4*	32	32	36
conventional low potency antipsychotic	4.7 (2.2)	*2*	28	36	36
divalproex	3.7 (2.2)	*3*	9	43	48
tricyclic antidepressant	3.2 (1.9)	*0*	7	30	62
carbamazepine	3.1 (1.8)	*0*	4	32	64
		%	%	%	%

* = *Treatment of Choice* ☐ = *No Consensus* *Note: 1st Line percentage includes Treatment of Choice percentage*

12 Please rate each of the following medications for an elderly patient with dementia and prominent ANGER. In this question, assume that *milder anger* is manifested verbally but does not include risk of physical aggression, while *severe anger* includes the risk of physical aggression. Please rate each medication separately for both short-term/p.r.n. and long-term use.

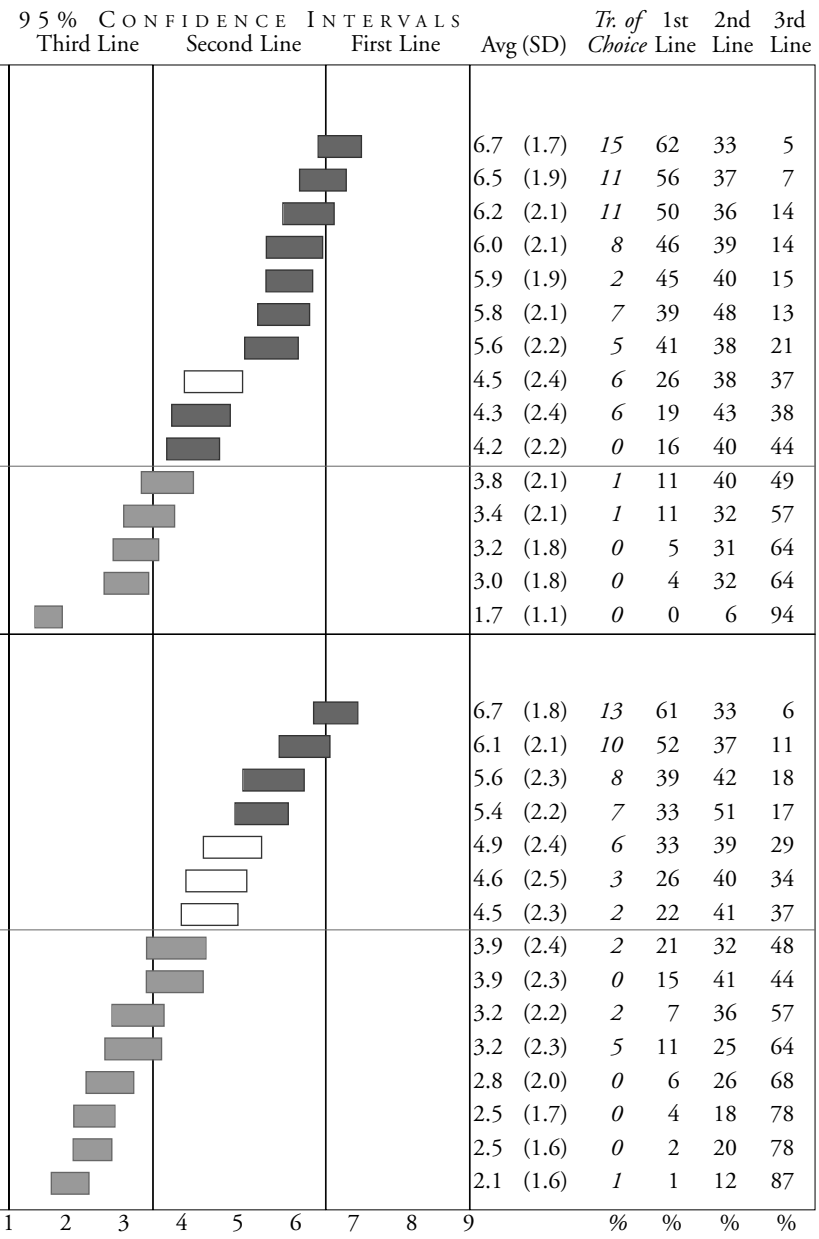
Comment: This question concerns anger or aggression that is not due to another prominent syndrome such as psychosis. For the long-term treatment of severe anger, there was no first line recommendation, but the experts give their top rating to divalproex, on the border of first line. A variety of other agents received high second line ratings, including atypical antipsychotics, conventional high potency antipsychotics, and several non-antipsychotics. For the short-term treatment of severe anger, the experts recommend conventional high potency antipsychotics, atypical antipsychotics, and trazodone. The experts have no strong medication recommendations for the short-term treatment of a patient with mild anger, suggesting the importance of environmental interventions for such patients. More persistent anger, even if mild, may benefit from long-term medication treatment with a variety of agents.



	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
LONG-TERM IN MILDER ANGER, NOT AGGRESSIVE					
divalproex	5.6 (2.3)	*10*	38	45	17
selective serotonin reuptake inhibitor	5.4 (2.2)	*10*	40	40	20
trazodone	5.4 (2.3)	*9*	35	51	15
buspirone	5.2 (2.1)	*9*	26	52	22
carbamazepine	4.9 (2.2)	*4*	23	46	30
risperidone	4.5 (2.2)	*1*	21	49	30
olanzapine	4.4 (2.4)	*6*	19	47	33
conventional high potency antipsychotic	4.0 (2.2)	*1*	12	52	36
beta-blocker	3.7 (2.2)	*2*	11	37	52
conventional low potency antipsychotic	3.4 (2.1)	*2*	9	37	54
other antidepressant	3.2 (1.9)	*0*	9	29	62
tricyclic antidepressant	3.1 (2.1)	*3*	6	33	61
benzodiazepine	3.1 (1.9)	*1*	5	30	65
clozapine	2.4 (1.7)	*1*	1	21	78
antihistamine	1.8 (1.1)	*0*	0	7	93
SHORT-TERM/P.R.N. IN MILDER ANGER, NOT AGGRESSIVE					
trazodone	5.1 (2.3)	*8*	28	51	22
benzodiazepine	4.5 (2.2)	*6*	23	43	34
conventional high potency antipsychotic	4.2 (2.2)	*1*	16	49	35
risperidone	4.2 (2.1)	*0*	18	46	36
olanzapine	4.0 (2.3)	*3*	16	41	42
selective serotonin reuptake inhibitor	3.8 (2.4)	*5*	16	33	52
divalproex	3.8 (2.3)	*0*	17	36	47
buspirone	3.4 (2.0)	*4*	7	37	55
carbamazepine	3.3 (2.2)	*0*	10	31	59
conventional low potency antipsychotic	3.3 (2.2)	*2*	11	30	59
beta-blocker	3.2 (2.1)	*2*	7	30	63
other antidepressant	2.5 (1.6)	*0*	4	20	77
tricyclic antidepressant	2.4 (1.6)	*0*	2	18	80
antihistamine	2.2 (1.6)	*1*	4	11	86
clozapine	2.0 (1.4)	*0*	0	15	85
		%	%	%	%

* = *Treatment of Choice* ☐ = *No Consensus* *Note: 1st Line percentage includes Treatment of Choice percentage*

12 *continued*



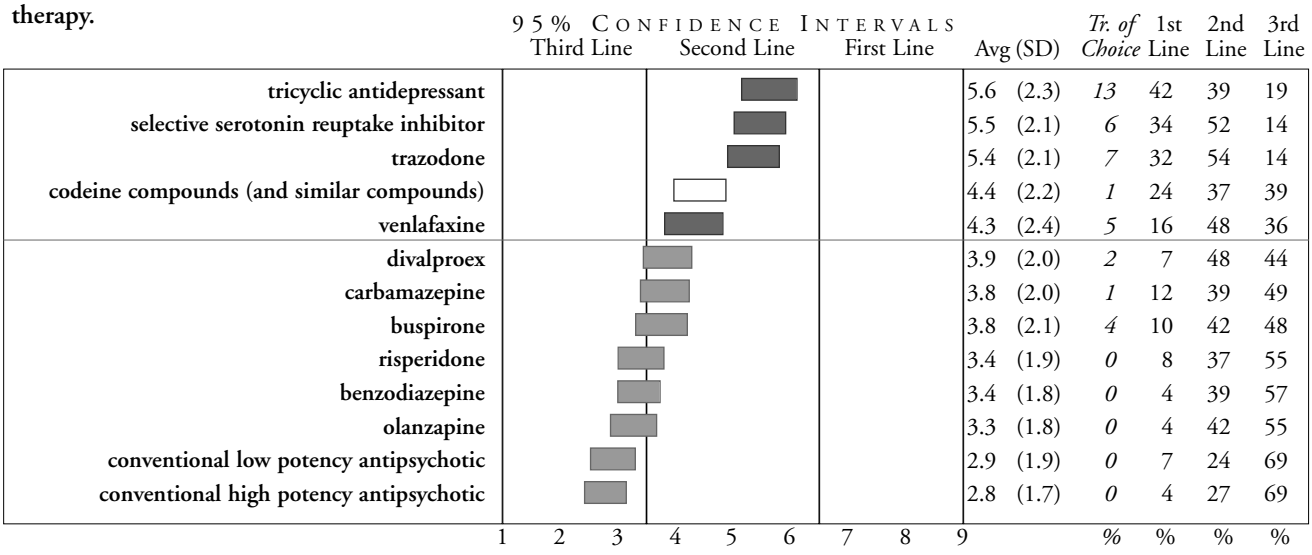
	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
Long-Term in Severe Anger with Aggression					
divalproex	6.7 (1.7)	*15*	62	33	5
risperidone	6.5 (1.9)	*11*	56	37	7
conventional high potency antipsychotic	6.2 (2.1)	*11*	50	36	14
olanzapine	6.0 (2.1)	*8*	46	39	14
carbamazepine	5.9 (1.9)	*2*	45	40	15
trazodone	5.8 (2.1)	*7*	39	48	13
selective serotonin reuptake inhibitor	5.6 (2.2)	*5*	41	38	21
buspirone	4.5 (2.4)	*6*	26	38	37
beta-blocker	4.3 (2.4)	*6*	19	43	38
conventional low potency antipsychotic	4.2 (2.2)	*0*	16	40	44
clozapine	3.8 (2.1)	*1*	11	40	49
benzodiazepine	3.4 (2.1)	*1*	11	32	57
other antidepressant	3.2 (1.8)	*0*	5	31	64
tricyclic antidepressant	3.0 (1.8)	*0*	4	32	64
antihistamine	1.7 (1.1)	*0*	0	6	94
Short-Term/P.R.N. in Severe Anger with Aggression					
conventional high potency antipsychotic	6.7 (1.8)	*13*	61	33	6
risperidone	6.1 (2.1)	*10*	52	37	11
olanzapine	5.6 (2.3)	*8*	39	42	18
trazodone	5.4 (2.2)	*7*	33	51	17
benzodiazepine	4.9 (2.4)	*6*	33	39	29
divalproex	4.6 (2.5)	*3*	26	40	34
conventional low potency antipsychotic	4.5 (2.3)	*2*	22	41	37
selective serotonin reuptake inhibitor	3.9 (2.4)	*2*	21	32	48
carbamazepine	3.9 (2.3)	*0*	15	41	44
beta-blocker	3.2 (2.2)	*2*	7	36	57
buspirone	3.2 (2.3)	*5*	11	25	64
clozapine	2.8 (2.0)	*0*	6	26	68
other antidepressant	2.5 (1.7)	*0*	4	18	78
tricyclic antidepressant	2.5 (1.6)	*0*	2	20	78
antihistamine	2.1 (1.6)	*1*	1	12	87
		%	*%*	*%*	*%*

* = *Treatment of Choice* ▭ = *No Consensus*

Note: 1st Line percentage includes Treatment of Choice percentage

13 Please rate the following interventions to alleviate AGITATION DUE TO CHRONIC OSTEOARTHRITIC PAIN in an elderly patient with dementia. Assume that the patient continues to have some pain despite maximum safe doses of nonsteroidal anti-inflammatory drugs or acetaminophen and use of appropriate positioning/physical therapy.

Comment: The tricyclic antidepressants (TCAs) receive lower ratings in other situations in which antidepressants might be used, but were more highly rated for the treatment of a patient with agitation due to chronic osteoarthritic pain. This probably reflects the literature, which suggests that TCAs may have a beneficial effect on pain. Note that the three types of antidepressants are preferred to codeine compounds.



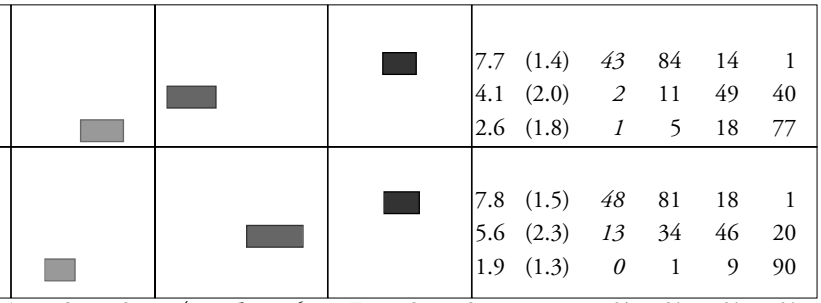
	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
tricyclic antidepressant	5.6 (2.3)	*13*	42	39	19
selective serotonin reuptake inhibitor	5.5 (2.1)	*6*	34	52	14
trazodone	5.4 (2.1)	*7*	32	54	14
codeine compounds (and similar compounds)	4.4 (2.2)	*1*	24	37	39
venlafaxine	4.3 (2.4)	*5*	16	48	36
divalproex	3.9 (2.0)	*2*	7	48	44
carbamazepine	3.8 (2.0)	*1*	12	39	49
buspirone	3.8 (2.1)	*4*	10	42	48
risperidone	3.4 (1.9)	*0*	8	37	55
benzodiazepine	3.4 (1.8)	*0*	4	39	57
olanzapine	3.3 (1.8)	*0*	4	42	55
conventional low potency antipsychotic	2.9 (1.9)	*0*	7	24	69
conventional high potency antipsychotic	2.8 (1.7)	*0*	4	27	69
		%	%	%	%

* = *Treatment of Choice* ☐ = *No Consensus*

Note: 1st Line percentage includes Treatment of Choice percentage

14 No Initial Response to Medication, next step: Suppose that your initial drug choice, at an adequate, tolerable dose, had little or no effect within your planned time range. Please rate the following general next steps.

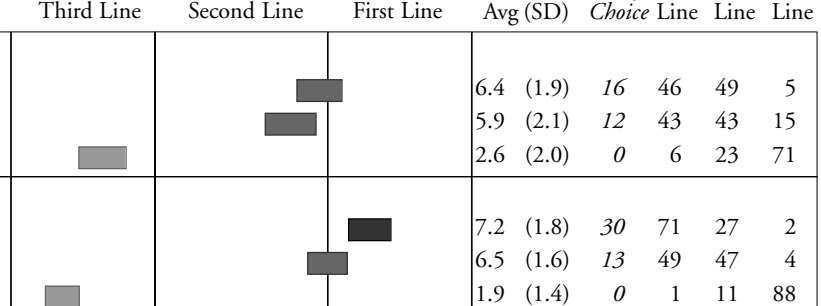
Comment: If a patient has had little or no response to an adequate trial of a medication, the experts' first line choice for both mild and more severe agitation is to switch to a second medication. The experts do not recommend combination therapy, which is associated with an increased risk of side effects for elderly patients, although this option receives somewhat better ratings for more severe agitation.



	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
Milder Agitation					
switch to a second medication	7.7 (1.4)	*43*	84	14	1
combine with a second medication	4.1 (2.0)	*2*	11	49	40
no further medication	2.6 (1.8)	*1*	5	18	77
Severe Agitation					
switch to a second medication	7.8 (1.5)	*48*	81	18	1
combine with a second medication	5.6 (2.3)	*13*	34	46	20
no further medication	1.9 (1.3)	*0*	1	9	90
		%	%	%	%

15 Partial Response to Medication, next step: Suppose that your initial drug choice, at an adequate, tolerable dose, produced a partial but unsatisfactory response within your planned time range. Please rate the following general next steps.

Comment: When a patient with mild agitation is having a partial but unsatisfactory response to a medication, the experts again recommend switching to another medication, followed by combining the first medication with another agent. However, when the agitation is more severe, the experts' first line recommendation is to try combination therapy, probably reflecting a reluctance to discontinue a medication that may be producing a partial response. However, if side effects were the limiting problem in continuing or raising a dose of medication, the editors suggest that it is probably preferable to switch to a second medication.

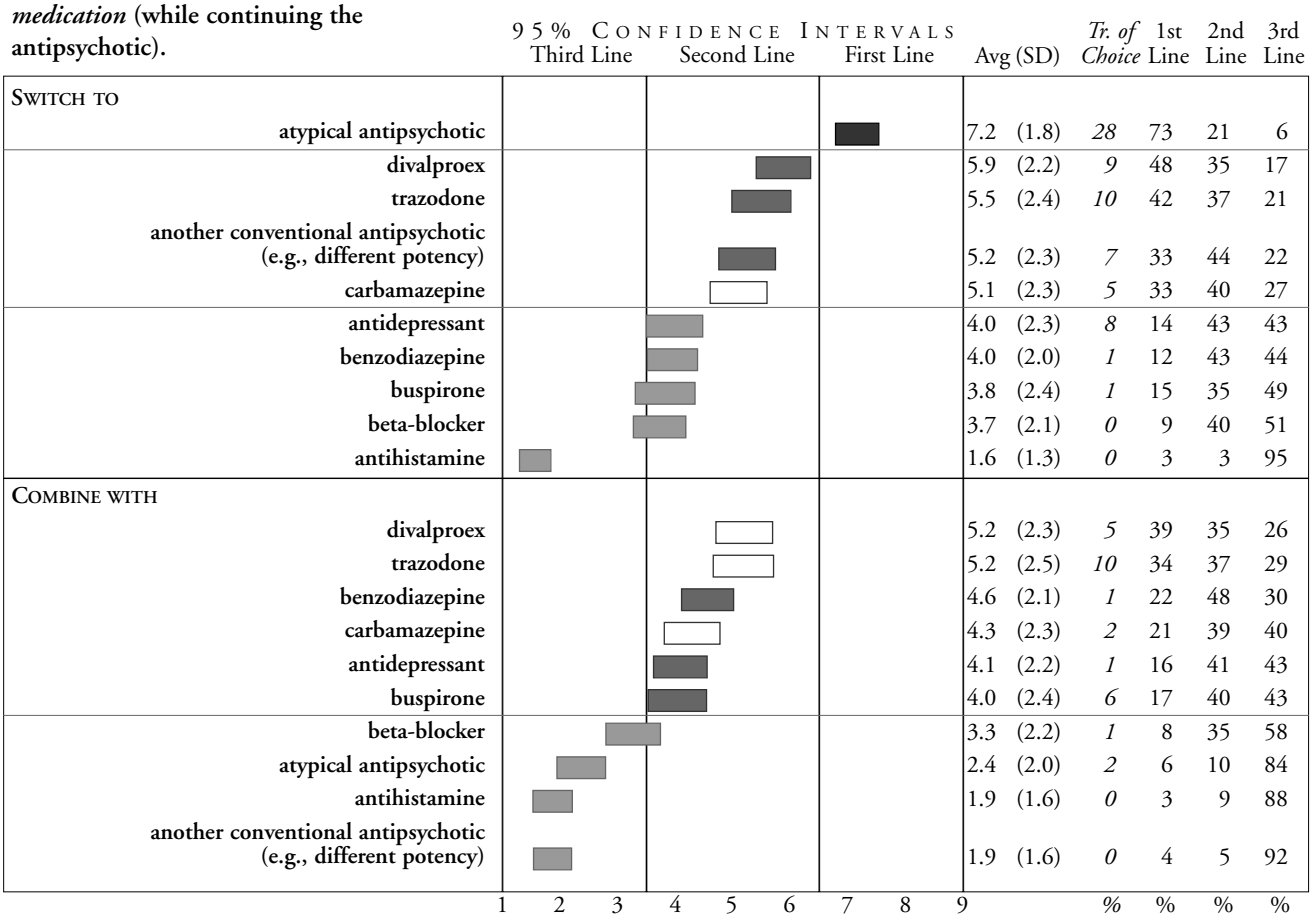


	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
Milder Agitation					
switch to a second medication	6.4 (1.9)	*16*	46	49	5
combine with a second medication	5.9 (2.1)	*12*	43	43	15
no further medication	2.6 (2.0)	*0*	6	23	71
Severe Agitation					
combine with a second medication	7.2 (1.8)	*30*	71	27	2
switch to a second medication	6.5 (1.6)	*13*	49	47	4
no further medication	1.9 (1.4)	*0*	1	11	88
		%	%	%	%

* = *Treatment of Choice* ☐ = *No Consensus* *Note: 1st Line percentage includes Treatment of Choice percentage*

16 TREATMENT RESISTANCE TO A CONVENTIONAL ANTIPSYCHOTIC: Assume you had initially treated an agitated patient with dementia with a conventional antipsychotic alone and had achieved little or no response at a maximum tolerated dose. Please rate each of the following choices for the next strategies: either to *switch medications* (while tapering the antipsychotic) or to *combine with a second medication* (while continuing the antipsychotic).

Comment: When a patient has failed to respond to a conventional antipsychotic, the experts' first line recommendation is to switch to an atypical antipsychotic, followed by switching to divalproex as the top second line recommendation. Switching to trazodone, another conventional antipsychotic, or possibly carbamazepine is another second line option. Combination strategies receive lower ratings, in keeping with the recommendations in Survey Question 14. If a combination strategy is used, note that a combination of two antipsychotics is considered generally inappropriate.



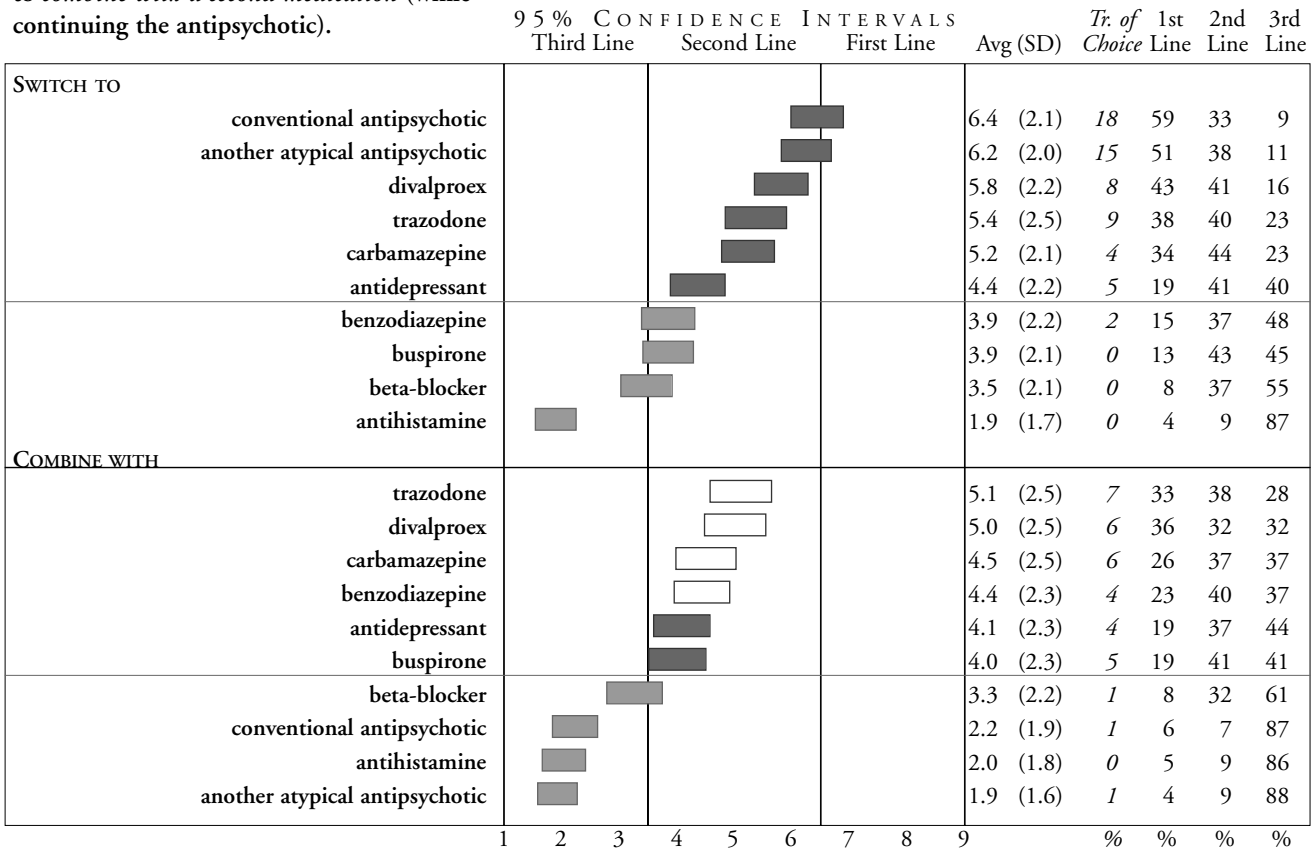
	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
SWITCH TO					
atypical antipsychotic	7.2 (1.8)	*28*	73	21	6
divalproex	5.9 (2.2)	*9*	48	35	17
trazodone	5.5 (2.4)	*10*	42	37	21
another conventional antipsychotic (e.g., different potency)	5.2 (2.3)	*7*	33	44	22
carbamazepine	5.1 (2.3)	*5*	33	40	27
antidepressant	4.0 (2.3)	*8*	14	43	43
benzodiazepine	4.0 (2.0)	*1*	12	43	44
buspirone	3.8 (2.4)	*1*	15	35	49
beta-blocker	3.7 (2.1)	*0*	9	40	51
antihistamine	1.6 (1.3)	*0*	3	3	95
COMBINE WITH					
divalproex	5.2 (2.3)	*5*	39	35	26
trazodone	5.2 (2.5)	*10*	34	37	29
benzodiazepine	4.6 (2.1)	*1*	22	48	30
carbamazepine	4.3 (2.3)	*2*	21	39	40
antidepressant	4.1 (2.2)	*1*	16	41	43
buspirone	4.0 (2.4)	*6*	17	40	43
beta-blocker	3.3 (2.2)	*1*	8	35	58
atypical antipsychotic	2.4 (2.0)	*2*	6	10	84
antihistamine	1.9 (1.6)	*0*	3	9	88
another conventional antipsychotic (e.g., different potency)	1.9 (1.6)	*0*	4	5	92
		%	%	%	%

* = *Treatment of Choice* = *No Consensus*

Note: 1st Line percentage includes Treatment of Choice percentage

17 Treatment Resistance to an Atypical Antipsychotic: Assume you had initially treated an agitated patient with dementia with an atypical antipsychotic alone and had achieved little or no response at a maximum tolerated dose. Please rate each of the following choices for the next strategies: either to *switch medications* (while tapering the antipsychotic) or to *combine with a second medication* (while continuing the antipsychotic).

Comment: When a patient has failed to respond to an atypical antipsychotic, the experts recommend switching to another agent rather than combining medications. With regard to what drug to switch to, the experts give similar ratings to a conventional antipsychotic or another atypical antipsychotic, followed by divalproex. Trazodone and carbamazepine are other alternatives.

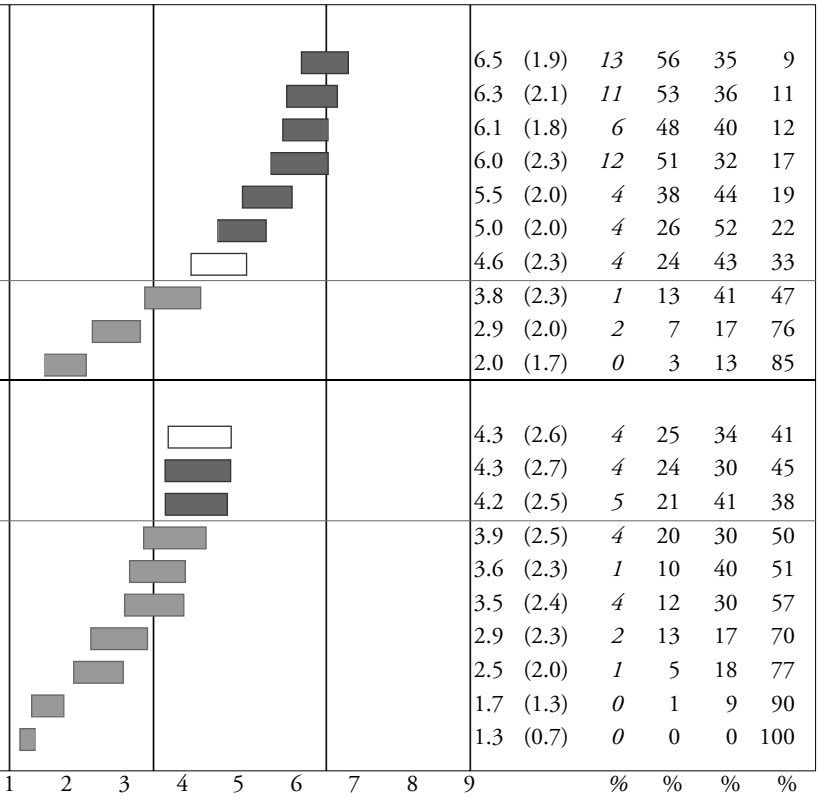


	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
Switch to					
conventional antipsychotic	6.4 (2.1)	*18*	59	33	9
another atypical antipsychotic	6.2 (2.0)	*15*	51	38	11
divalproex	5.8 (2.2)	*8*	43	41	16
trazodone	5.4 (2.5)	*9*	38	40	23
carbamazepine	5.2 (2.1)	*4*	34	44	23
antidepressant	4.4 (2.2)	*5*	19	41	40
benzodiazepine	3.9 (2.2)	*2*	15	37	48
buspirone	3.9 (2.1)	*0*	13	43	45
beta-blocker	3.5 (2.1)	*0*	8	37	55
antihistamine	1.9 (1.7)	*0*	4	9	87
Combine with					
trazodone	5.1 (2.5)	*7*	33	38	28
divalproex	5.0 (2.5)	*6*	36	32	32
carbamazepine	4.5 (2.5)	*6*	26	37	37
benzodiazepine	4.4 (2.3)	*4*	23	40	37
antidepressant	4.1 (2.3)	*4*	19	37	44
buspirone	4.0 (2.3)	*5*	19	41	41
beta-blocker	3.3 (2.2)	*1*	8	32	61
conventional antipsychotic	2.2 (1.9)	*1*	6	7	87
antihistamine	2.0 (1.8)	*0*	5	9	86
another atypical antipsychotic	1.9 (1.6)	*1*	4	9	88
		%	%	%	%

* = *Treatment of Choice* ☐ = *No Consensus* *Note: 1st Line percentage includes Treatment of Choice percentage*

18 TREATMENT RESISTANCE TO A BENZODIAZEPINE: Assume you had initially treated a patient with a benzodiazepine alone and had achieved little or no response at a maximum tolerated dose. Please rate each of the following choices for the next strategies: either to *switch medications* (while tapering the benzodiazepine) or to *combine with a second medication* (while continuing the benzodiazepine).

Comment: When a patient has failed to respond to a benzodiazepine, the experts again recommend switching to another agent rather than combining medications. The experts suggest a variety of different medications in this situation: an atypical or conventional antipsychotic, divalproex, or trazodone, followed by carbamazepine or an antidepressant.



	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
SWITCH TO					
atypical antipsychotic	6.5 (1.9)	*13*	56	35	9
conventional antipsychotic	6.3 (2.1)	*11*	53	36	11
divalproex	6.1 (1.8)	*6*	48	40	12
trazodone	6.0 (2.3)	*12*	51	32	17
carbamazepine	5.5 (2.0)	*4*	38	44	19
antidepressant	5.0 (2.0)	*4*	26	52	22
buspirone	4.6 (2.3)	*4*	24	43	33
beta-blocker	3.8 (2.3)	*1*	13	41	47
another benzodiazepine	2.9 (2.0)	*2*	7	17	76
antihistamine	2.0 (1.7)	*0*	3	13	85
COMBINE WITH					
conventional antipsychotic	4.3 (2.6)	*4*	25	34	41
divalproex	4.3 (2.7)	*4*	24	30	45
atypical antipsychotic	4.2 (2.5)	*5*	21	41	38
trazodone	3.9 (2.5)	*4*	20	30	50
antidepressant	3.6 (2.3)	*1*	10	40	51
carbamazepine	3.5 (2.4)	*4*	12	30	57
buspirone	2.9 (2.3)	*2*	13	17	70
beta-blocker	2.5 (2.0)	*1*	5	18	77
antihistamine	1.7 (1.3)	*0*	1	9	90
another benzodiazepine	1.3 (0.7)	*0*	0	0	100
		%	%	%	%

* = *Treatment of Choice* ☐ = *No Consensus* *Note: 1st Line percentage includes Treatment of Choice percentage*

19 Selection of P.R.N. Medication to Combine with Other Medications: Assume you are treating a patient with a beta-blocker, buspirone, carbamazepine, divalproex, or a selective serotonin reuptake inhibitor, and that you have decided you need a second medication as a p.r.n. sedative for episodes of breakthrough agitation. Please rate each of the following medications as an add-on p.r.n. choice.

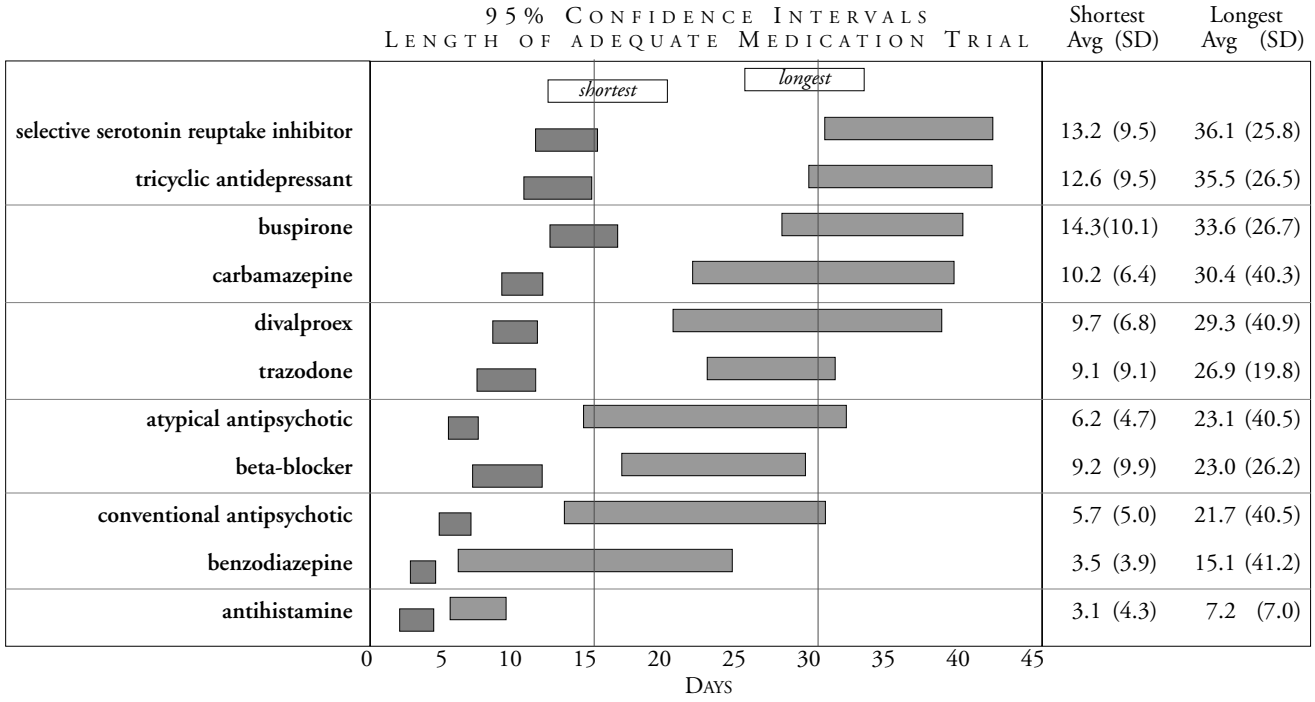
Comment: The experts show little enthusiasm for adding a sedating medication for mild episodes of breakthrough agitation. For more severe agitation, they give higher ratings to using an antipsychotic or a benzodiazepine to produce short-term sedation.

	95% Confidence Intervals				*Tr. of Choice*	1st Line	2nd Line	3rd Line
	Third Line	Second Line	First Line	Avg (SD)				
Milder Agitation								
benzodiazepine				5.8 (2.5)	*13*	50	27	23
trazodone				5.3 (2.6)	*15*	32	42	26
conventional antipsychotic				5.0 (2.0)	*2*	26	49	26
atypical antipsychotic				4.5 (2.2)	*2*	21	46	33
antihistamine				2.6 (2.2)	*1*	10	19	71
Severe Agitation								
conventional antipsychotic				6.8 (1.6)	*13*	64	31	5
benzodiazepine				6.2 (2.3)	*16*	53	31	16
atypical antipsychotic				6.0 (2.4)	*12*	54	29	17
trazodone				5.1 (2.6)	*10*	33	38	29
antihistamine				2.2 (1.8)	*0*	5	11	84
	1 2 3	4 5 6	7 8 9		*%*	%	%	%

* = *Treatment of Choice* = *No Consensus* *Note: 1st Line percentage includes Treatment of Choice percentage*

20 LENGTH OF AN ADEQUATE MEDICATION TRIAL: Suppose you are not yet seeing an adequate response to continuous medication for agitation in an elderly patient with dementia in a nonurgent situation (with an adequate response defined as the clinician being satisfied with both the rate and absolute degree of symptom reduction after an appropriate dose is achieved). What are the *shortest* and *longest* times you would wait, from the time you initiated treatment with each of the following medications, before trying a different plan (e.g., switching to or adding another medication)? Assume you have raised the dose as rapidly as possible to an appropriate, tolerable level.

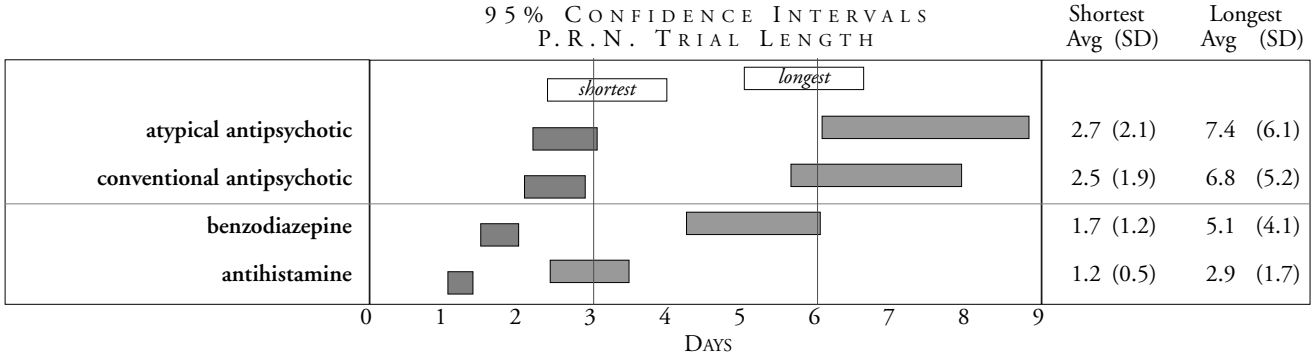
Comment: Medications for long-term treatment of agitation vary in the time it takes before clinical effects are seen (the minimum duration for a therapeutic trial), or before it can be determined that they are unlikely to produce benefit (the maximum duration one should wait before trying another plan). Divalproex, buspirone, selective serotonin reuptake inhibitors, and tricyclic antidepressants appear to take at least 10 to 14 days to begin working and may take up to 4 or 5 weeks. Carbamazepine may show effects slightly earlier, but if not, it may also be continued for up to a month. Trazodone may work more quickly, showing effects within 1 week, but a trial may last as long as 3 or 4 weeks. Antipsychotics work still more rapidly, taking from a few days to a few weeks. Benzodiazepines and antihistamines appear to deserve the shortest trials. (Antihistamines are not recommended in the other questions where we asked about them.)



* = *Treatment of Choice* = *No Consensus* *Note: 1st Line percentage includes Treatment of Choice percentage*

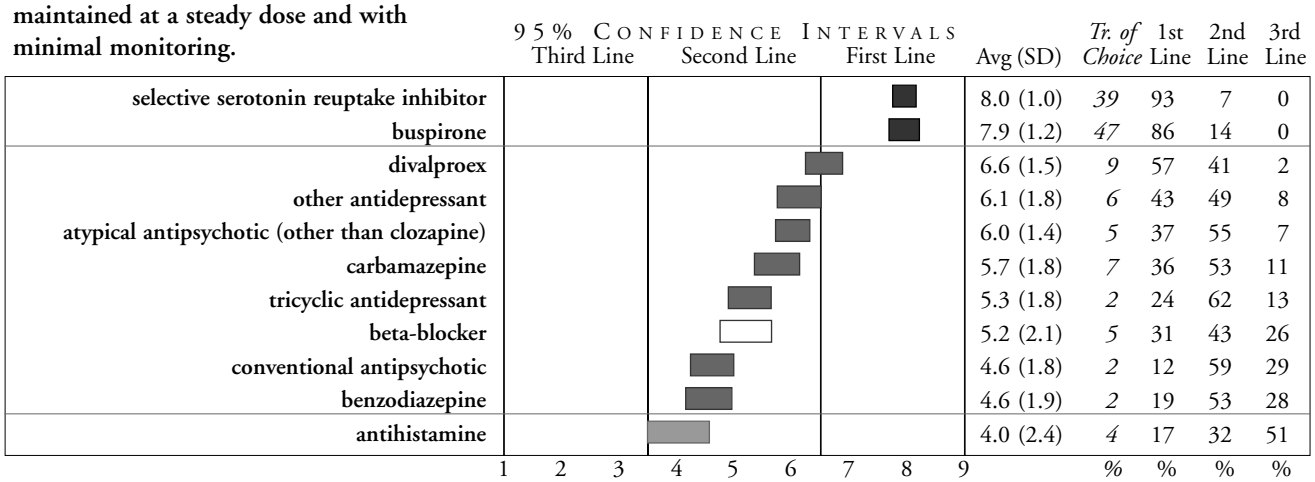
21 P.R.N. TRIAL LENGTH: Suppose you are seeking a rapid, short-term response in an urgent situation. What are the *shortest* and *longest* periods (in days) you would wait, from the time you initiated treatment with each of the following medications, before trying a different plan (e.g., switching to or adding another medication)? Assume you are using the maximum tolerable dosing schedule. Please cross out choices that you would *not* consider using in a p.r.n. fashion.

Comment: In urgent situations, a single dose may not be adequate to judge a response, especially if treatment begins with a very low dose. The panel estimates that it may take from 2 to 3 days up to a week, using p.r.n. doses of conventional or atypical antipsychotics (presumably with careful dose titration), to judge efficacy. Benzodiazepines take somewhat less time to demonstrate whether or not they will help.



22 LONG-TERM SAFETY: Federal regulations (OBRA, 1987; HCFA guidelines) state, for patients in nursing homes, that treatment with certain classes of psychotropic medication requires an attempt at dose reduction at least twice per year and that side effects be continuously monitored and documented. Based on your experience and opinion, please rate the following choices for long-term safety, giving your highest ratings to those medications least likely to cause serious problems if maintained at a steady dose and with minimal monitoring.

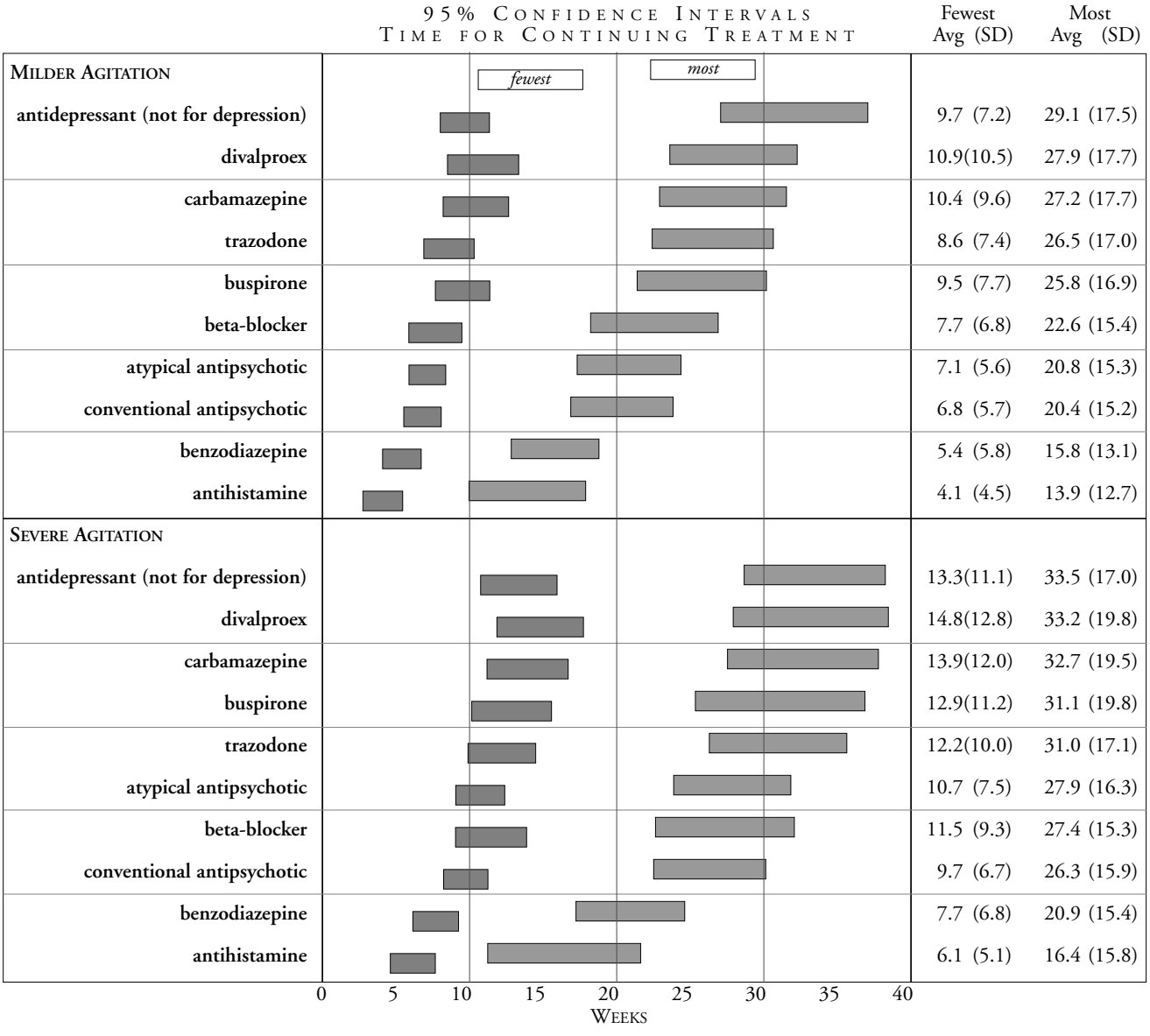
Comment: For long-term safety, the experts' first line preferences are the selective serotonin reuptake inhibitors (SSRIs) and buspirone. Among the anticonvulsants, the experts judge divalproex to have the best long-term safety profile. Among antipsychotics, there is a significant preference for atypical rather than conventional antipsychotics for long-term use. Among the antidepressants, the SSRIs are preferred over the traditional tricyclic antidepressants, with other new antidepressants rated somewhere in between. Although the category "other antidepressants" would include the monoamine oxidase inhibitors (MAOIs), we assume the experts were referring to the other newer antidepressants in their response to this question, since a clinician would be extremely unlikely to use an MAOI in an elderly patient with dementia. The experts have serious reservations about the safety of long-term benzodiazepine use.



* = Treatment of Choice = No Consensus *Note: 1st Line percentage includes Treatment of Choice percentage*

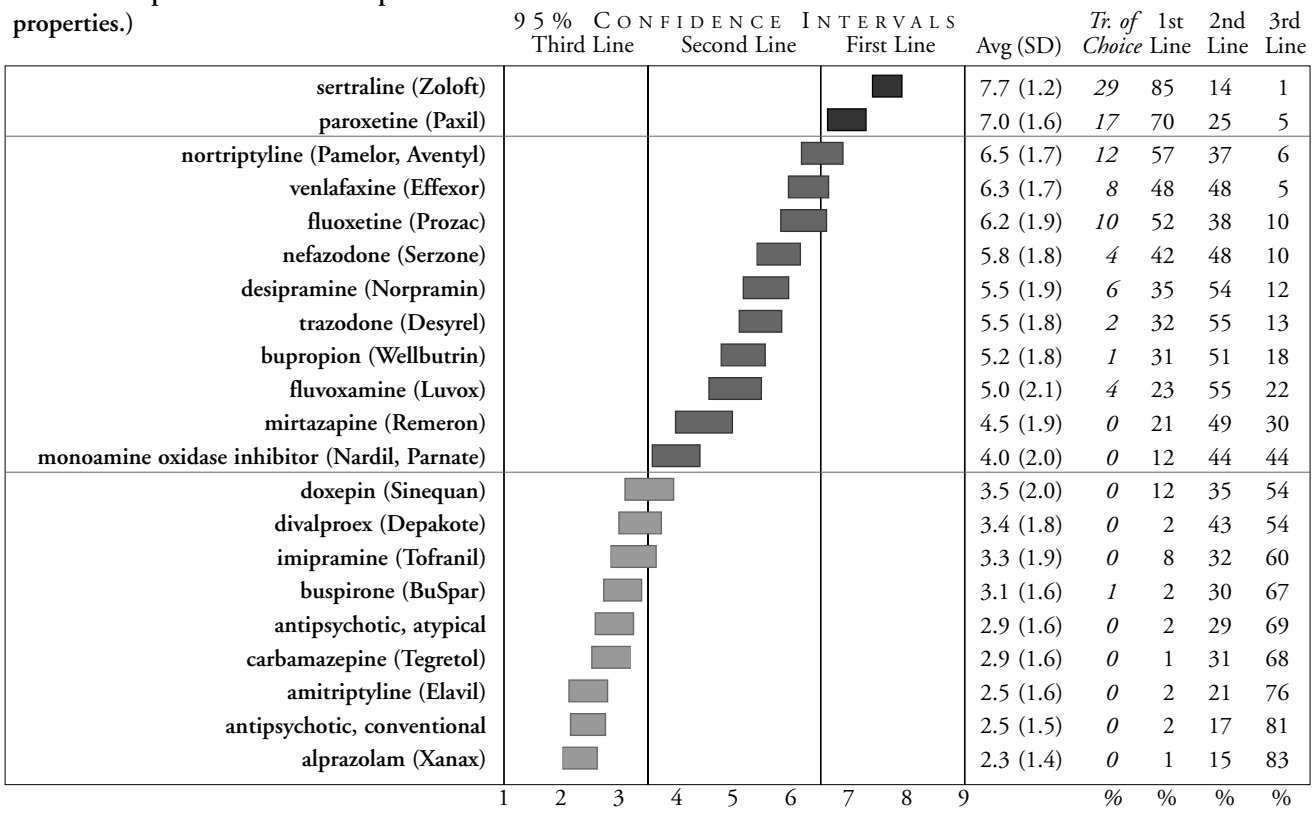
23 TIME COURSE FOR CONTINUING A SUCCESSFUL TREATMENT: Suppose a medication has been working well for at least a few weeks in an elderly patient with dementia who had been chronically agitated with no underlying, reversible cause. Assume that this treatment episode is the first time the patient has received a trial of anti-agitation medication. How long would you continue medication before attempting to taper and discontinue it? Please fill in the range of weeks, beginning at the point where the patient has reached a satisfactory plateau of improvement. If you would usually continue a medication indefinitely with no plan to taper it off, please mark the blank space with an "XX."

Comment: If a patient has responded well to a medication, the experts advise trying to taper and discontinue it after a range of time, which depends on the type of medication and severity of the prior agitation. Divalproex, carbamazepine, antidepressants if used for agitation (as opposed to depression), and buspirone can be continued for an average of about 2 to 4 months in milder agitation and 3.5 to 8 months in more severe agitation. Antipsychotics (and beta-blockers, although rarely used) can be continued for about 2 to 5 months in milder agitation and about 2.5 to 7 months in severe agitation. Benzodiazepines (and antihistamines, although rarely used) are continued for the shortest times, from 4 to 6 weeks up to 3 to 4 months in milder agitation and 2 to 5 months in severe agitation.



24 Assume that you have decided to use a medication to treat DEPRESSIVE SYMPTOMS in an elderly person with dementia and agitation. Please give your highest ratings to those choices that you believe are both effective in alleviating depression and reasonably well tolerated. (We have listed several choices that are not identified as antidepressants but that are sometimes reported to have antidepressant properties.)

Comment: The experts' first line choice for an antidepressant is sertraline, followed by paroxetine. These agents can be administered once a day and have relatively few dangerous side effects. The top second line choices are nonsedating tricyclic antidepressants (TCAs) and a host of newer antidepressants. The sedating TCAs (e.g., amitriptyline, doxepin, imipramine) receive much lower ratings, probably because of concern about orthostatic hypotension, anticholinergic-induced confusion, and sedation.



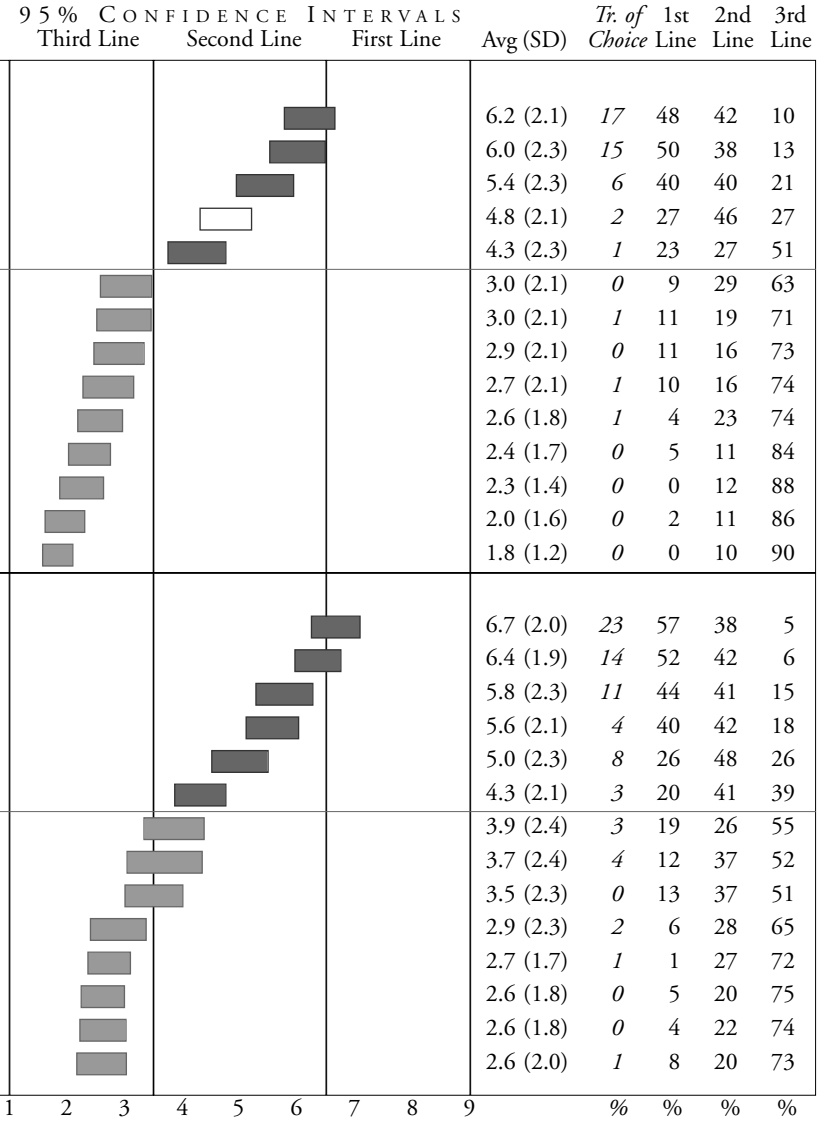
	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
sertraline (Zoloft)	7.7 (1.2)	*29*	85	14	1
paroxetine (Paxil)	7.0 (1.6)	*17*	70	25	5
nortriptyline (Pamelor, Aventyl)	6.5 (1.7)	*12*	57	37	6
venlafaxine (Effexor)	6.3 (1.7)	*8*	48	48	5
fluoxetine (Prozac)	6.2 (1.9)	*10*	52	38	10
nefazodone (Serzone)	5.8 (1.8)	*4*	42	48	10
desipramine (Norpramin)	5.5 (1.9)	*6*	35	54	12
trazodone (Desyrel)	5.5 (1.8)	*2*	32	55	13
bupropion (Wellbutrin)	5.2 (1.8)	*1*	31	51	18
fluvoxamine (Luvox)	5.0 (2.1)	*4*	23	55	22
mirtazapine (Remeron)	4.5 (1.9)	*0*	21	49	30
monoamine oxidase inhibitor (Nardil, Parnate)	4.0 (2.0)	*0*	12	44	44
doxepin (Sinequan)	3.5 (2.0)	*0*	12	35	54
divalproex (Depakote)	3.4 (1.8)	*0*	2	43	54
imipramine (Tofranil)	3.3 (1.9)	*0*	8	32	60
buspirone (BuSpar)	3.1 (1.6)	*1*	2	30	67
antipsychotic, atypical	2.9 (1.6)	*0*	2	29	69
carbamazepine (Tegretol)	2.9 (1.6)	*0*	1	31	68
amitriptyline (Elavil)	2.5 (1.6)	*0*	2	21	76
antipsychotic, conventional	2.5 (1.5)	*0*	2	17	81
alprazolam (Xanax)	2.3 (1.4)	*0*	1	15	83
		%	%	%	%

* = *Treatment of Choice* ☐ = *No Consensus* *Note: 1st Line percentage includes Treatment of Choice percentage*

25 Assume you have decided to use a SEDATIVE-HYPNOTIC or ANXIOLYTIC in an elderly patient with dementia and agitation. Please rate each of the following choices for two different uses: generalized agitation that occurs day or night and nighttime use only when you are trying to promote sleep in an agitated patient while avoiding daytime effects. Assume that the patient is able to take the medication by mouth.

Comment: Benzodiazepines are not a first line treatment for insomnia in this population (see Survey Question 10). However, when benzodiazepines are indicated, the experts prefer agents that have relatively short half-lives (e.g., 8 to 12 hours) and simple metabolism (zolpidem, lorazepam, temazepam, and oxazepam). The three hydroxybenzodiazepines (lorazepam, temazepam, and oxazepam) do not undergo Phase 1 metabolism in the liver; instead, they are conjugated with glucuronide and then excreted. For this reason, their clearance is minimally affected by aging. Note that a number of commonly used benzodiazepines that are generally longer-acting (e.g., flurazepam, clorazepate, chlordiazepoxide, diazepam) are not recommended for use in the elderly.

The experts' recommendation for sedative-hypnotics or anxiolytics for generalized agitation should be considered in conjunction with the recommendations in Survey Question 9. For long-term management of agitation characterized by generalized anxiety, the experts prefer buspirone, followed by trazodone and selective serotonin reuptake inhibitors. Benzodiazepines are acceptable for acute treatment of agitation characterized by prominent generalized anxiety. In selecting a sedative-hypnotic or an anxiolytic for generalized agitation that occurs day or night, the experts prefer lorazepam and buspirone.

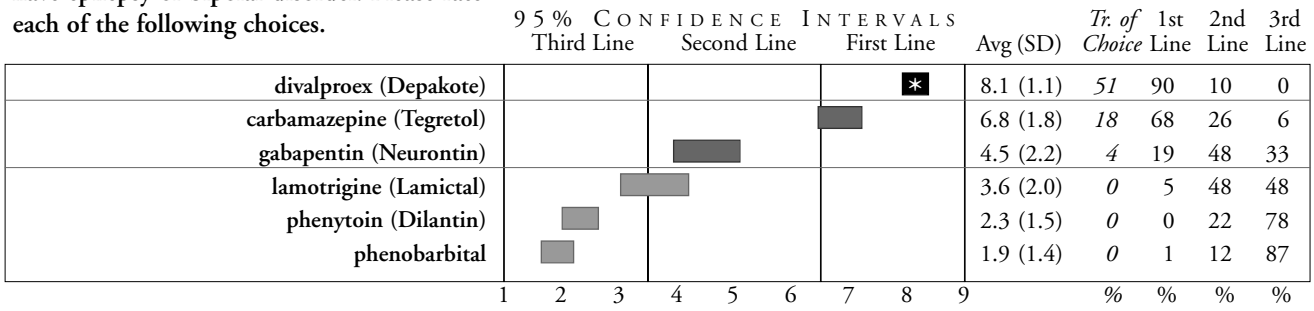


	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
GENERAL USE					
lorazepam (Ativan)	6.2 (2.1)	*17*	48	42	10
buspirone (BuSpar)	6.0 (2.3)	*15*	50	38	13
oxazepam (Serax)	5.4 (2.3)	*6*	40	40	21
clonazepam (Klonopin)	4.8 (2.1)	*2*	27	46	27
alprazolam (Xanax)	4.3 (2.3)	*1*	23	27	51
temazepam (Restoril)	3.0 (2.1)	*0*	9	29	63
clorazepate (Tranxene)	3.0 (2.1)	*1*	11	19	71
chlordiazepoxide (Librium)	2.9 (2.1)	*0*	11	16	73
diazepam (Valium)	2.7 (2.1)	*1*	10	16	74
zolpidem (Ambien)	2.6 (1.8)	*1*	4	23	74
chloral hydrate (Noctec)	2.4 (1.7)	*0*	5	11	84
estazolam (ProSom)	2.3 (1.4)	*0*	0	12	88
flurazepam (Dalmane)	2.0 (1.6)	*0*	2	11	86
triazolam (Halcion)	1.8 (1.2)	*0*	0	10	90
NIGHT, SLEEP-PROMOTING					
zolpidem (Ambien)	6.7 (2.0)	*23*	57	38	5
lorazepam (Ativan)	6.4 (1.9)	*14*	52	42	6
temazepam (Restoril)	5.8 (2.3)	*11*	44	41	15
oxazepam (Serax)	5.6 (2.1)	*4*	40	42	18
chloral hydrate (Noctec)	5.0 (2.3)	*8*	26	48	26
clonazepam (Klonopin)	4.3 (2.1)	*3*	20	41	39
alprazolam (Xanax)	3.9 (2.4)	*3*	19	26	55
estazolam (ProSom)	3.7 (2.4)	*4*	12	37	52
triazolam (Halcion)	3.5 (2.3)	*0*	13	37	51
flurazepam (Dalmane)	2.9 (2.3)	*2*	6	28	65
buspirone (BuSpar)	2.7 (1.7)	*1*	1	27	72
chlordiazepoxide (Librium)	2.6 (1.8)	*0*	5	20	75
clorazepate (Tranxene)	2.6 (1.8)	*0*	4	22	74
diazepam (Valium)	2.6 (2.0)	*1*	8	20	73
		%	%	%	%

* = *Treatment of Choice* = *No Consensus* *Note: 1st Line percentage includes Treatment of Choice percentage*

26 In any of the preceding situations, assume you have decided to use an ANTICONVULSANT to control agitation in an elderly patient with dementia who does not have epilepsy or bipolar disorder. Please rate each of the following choices.

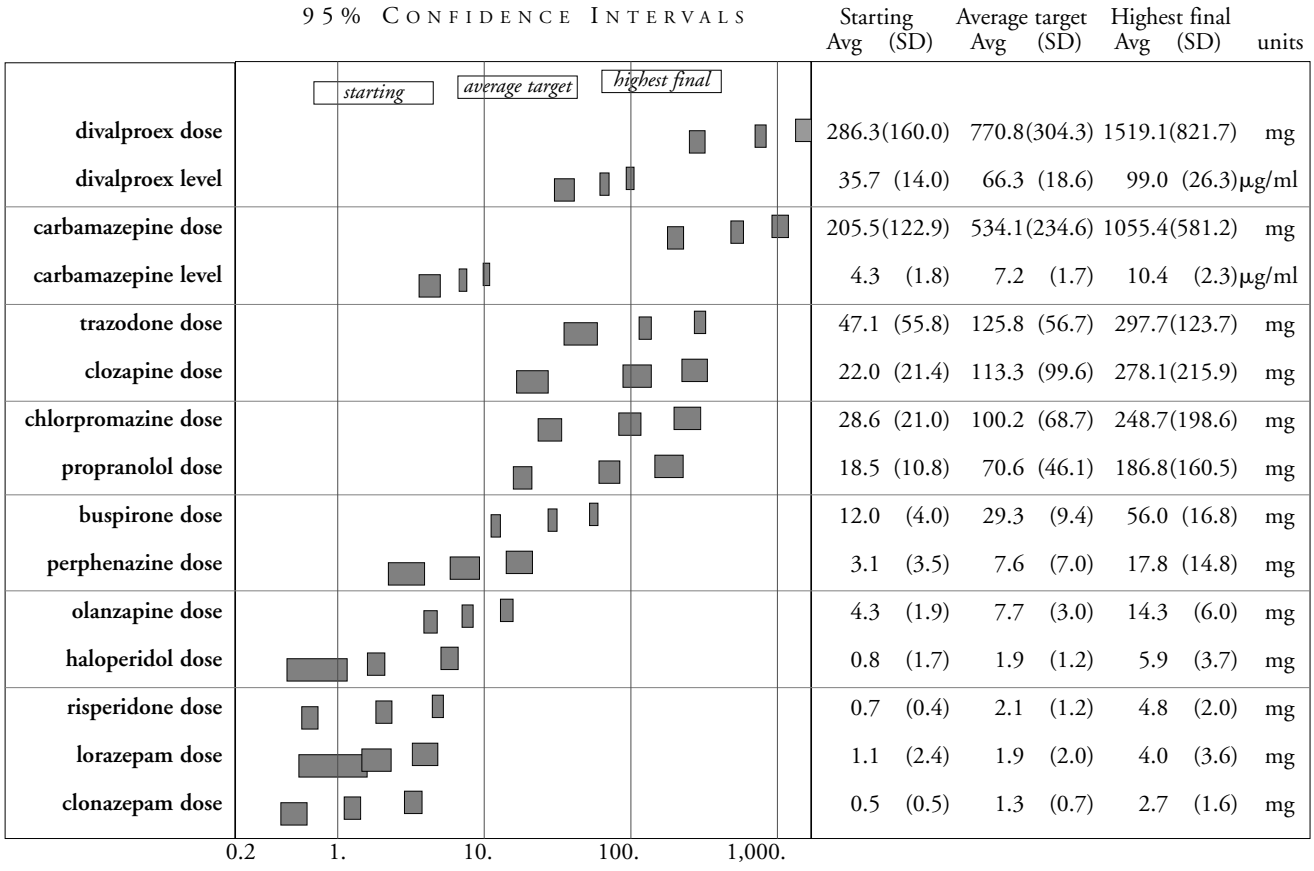
Comment: Anticonvulsants are an important treatment option for the long-term treatment of psychosis that has not responded to antipsychotic treatment (see Survey Question 6) and the long-term treatment of aggressive anger (see Survey Question 12). Among the anticonvulsants, divalproex is the treatment of choice, with carbamazepine the preferred second line option.



	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
divalproex (Depakote)	8.1 (1.1)	*51*	90	10	0
carbamazepine (Tegretol)	6.8 (1.8)	*18*	68	26	6
gabapentin (Neurontin)	4.5 (2.2)	*4*	19	48	33
lamotrigine (Lamictal)	3.6 (2.0)	*0*	5	48	48
phenytoin (Dilantin)	2.3 (1.5)	*0*	0	22	78
phenobarbital	1.9 (1.4)	*0*	1	12	87
		%	%	%	%

27 ADEQUATE DOSE: Please write in the dose range (total mg per 24 hours) or blood level (where indicated) you recommend for each of the following medications in order to attempt an adequate trial in an agitated elderly patient with dementia. Assume you are giving the medication at least daily for a week or more, not on an episodic or p.r.n. basis.

Comment: Dosing of medications should be highly individualized to the response and side effects that occur in each patient. The panel clearly believes that starting doses should be much lower than the average dose one expects to reach eventually. In most cases, starting and average doses are much lower than the doses one would use for younger patients. The maximum doses shown approach the standards for younger patients but would rarely be needed in older persons.

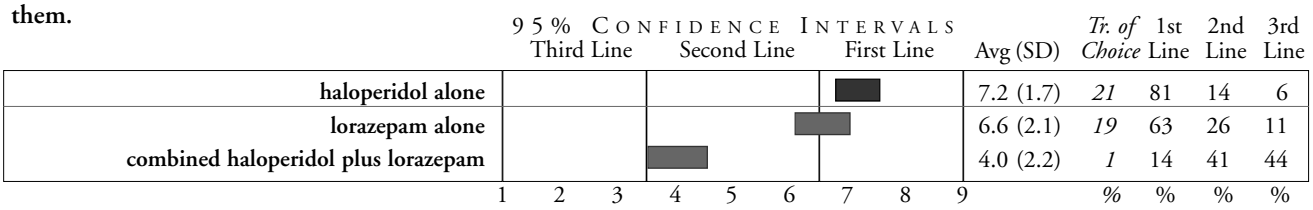


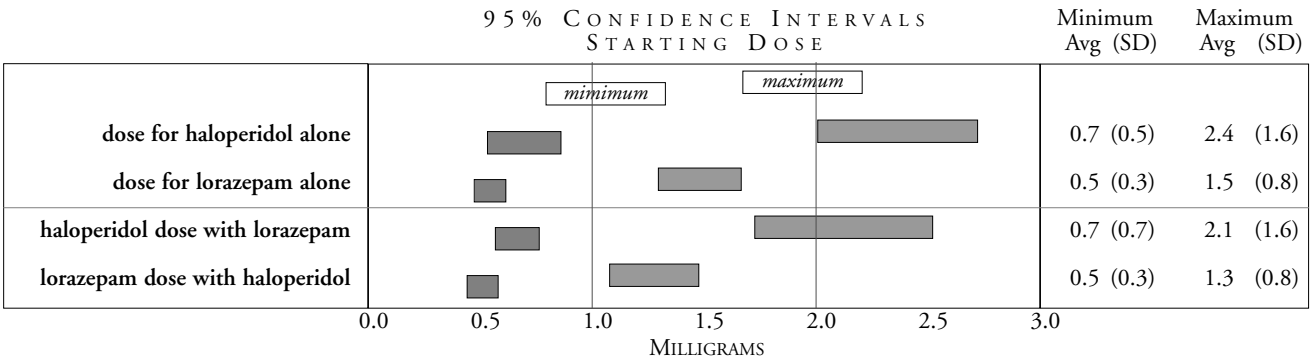
	Starting Avg (SD)	Average target Avg (SD)	Highest final Avg (SD)	units
divalproex dose	286.3(160.0)	770.8(304.3)	1519.1(821.7)	mg
divalproex level	35.7 (14.0)	66.3 (18.6)	99.0 (26.3)	µg/ml
carbamazepine dose	205.5(122.9)	534.1(234.6)	1055.4(581.2)	mg
carbamazepine level	4.3 (1.8)	7.2 (1.7)	10.4 (2.3)	µg/ml
trazodone dose	47.1 (55.8)	125.8 (56.7)	297.7(123.7)	mg
clozapine dose	22.0 (21.4)	113.3 (99.6)	278.1(215.9)	mg
chlorpromazine dose	28.6 (21.0)	100.2 (68.7)	248.7(198.6)	mg
propranolol dose	18.5 (10.8)	70.6 (46.1)	186.8(160.5)	mg
buspirone dose	12.0 (4.0)	29.3 (9.4)	56.0 (16.8)	mg
perphenazine dose	3.1 (3.5)	7.6 (7.0)	17.8 (14.8)	mg
olanzapine dose	4.3 (1.9)	7.7 (3.0)	14.3 (6.0)	mg
haloperidol dose	0.8 (1.7)	1.9 (1.2)	5.9 (3.7)	mg
risperidone dose	0.7 (0.4)	2.1 (1.2)	4.8 (2.0)	mg
lorazepam dose	1.1 (2.4)	1.9 (2.0)	4.0 (3.6)	mg
clonazepam dose	0.5 (0.5)	1.3 (0.7)	2.7 (1.6)	mg

= *Treatment of Choice* = *No Consensus* *Note: 1st Line percentage includes Treatment of Choice percentage*

28 Suppose you have decided to give an INTRAMUSCULAR (IM) MEDICATION for short-term/p.r.n. use in an elderly patient with dementia who has developed severe agitation but is otherwise medically stable. Please rate each of the following representative choices *and* indicate the range of starting doses you generally use in each scenario. Please provide this information for all three options, even if you rarely use them.

Comment: The experts' first line choice for short-term IM medication is haloperidol alone, at a dose range of 0.7 to 2.4 mg. Lorazepam is the experts' second line choice for IM use, at a dose range of 0.5 to 1.5 mg. Benzodiazepine treatment probably received higher ratings here than in other situations because the question describes what is likely to be an emergency situation in which the clinician wants to achieve quick sedation. As elsewhere in the survey, the experts recommend avoiding combination treatment in the elderly. In patients who have never taken these medications, the editors would recommend never using a higher initial dose than 1 mg. Higher doses would only be considered if information were available from the patient's previous history concerning response to and tolerance of higher doses.

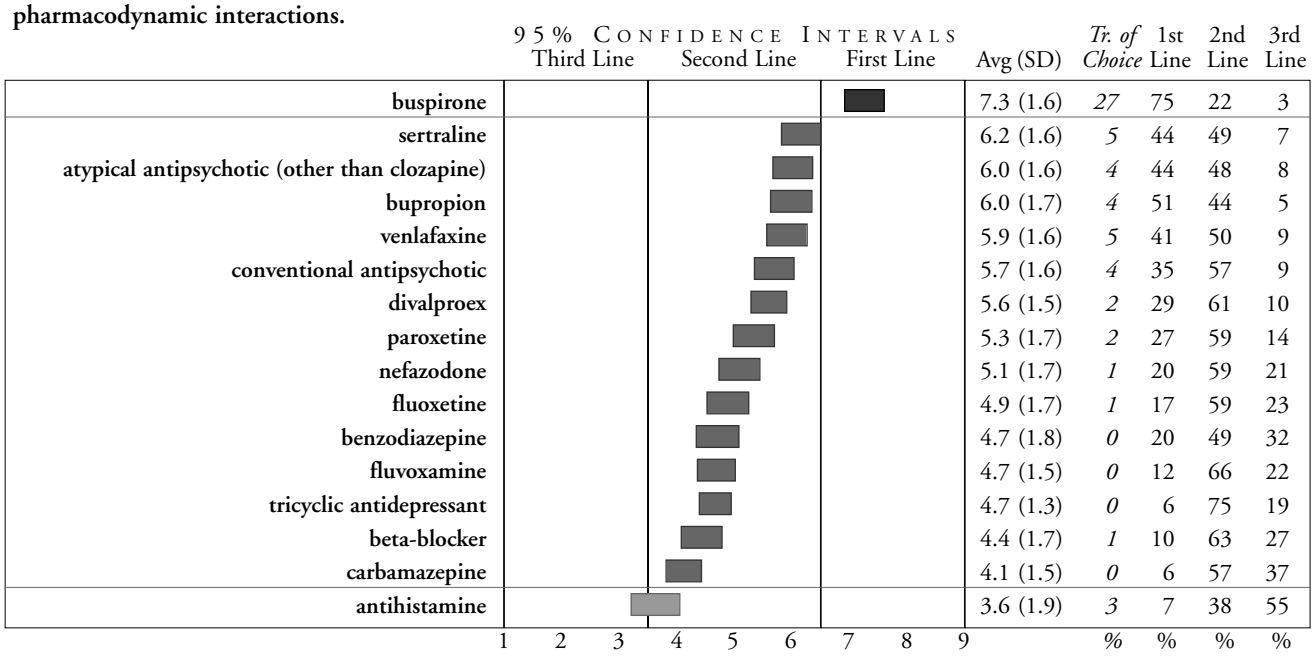




* = *Treatment of Choice* = *No Consensus* *Note: 1st Line percentage includes Treatment of Choice percentage*

29 Elderly patients sometimes receive multiple medications from multiple prescribers, often without optimal communication. Please rate each of the following for safety in AVOIDING DRUG INTERACTIONS in an agitated elderly patient with dementia who may be taking multiple medications. Please give ratings in the 7–9 range for the choice(s) *least likely in general* to cause significant pharmacokinetic *or* pharmacodynamic interactions.

Comment: The experts' first line choice for safety in a patient receiving multiple medications is buspirone. Several of the newer antidepressants were also rated as unlikely to cause significant pharmacokinetic or pharmacodynamic interactions. The experts are also comfortable with atypical antipsychotics and, to a somewhat lesser degree, with conventional antipsychotics. Among the anticonvulsants, they much prefer divalproex to carbamazepine. Note that several classes of medication, in particular tricyclic antidepressants and benzodiazepines, are a cause for concern in regard to drug interactions.



	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
buspirone	7.3 (1.6)	*27*	75	22	3
sertraline	6.2 (1.6)	*5*	44	49	7
atypical antipsychotic (other than clozapine)	6.0 (1.6)	*4*	44	48	8
bupropion	6.0 (1.7)	*4*	51	44	5
venlafaxine	5.9 (1.6)	*5*	41	50	9
conventional antipsychotic	5.7 (1.6)	*4*	35	57	9
divalproex	5.6 (1.5)	*2*	29	61	10
paroxetine	5.3 (1.7)	*2*	27	59	14
nefazodone	5.1 (1.7)	*1*	20	59	21
fluoxetine	4.9 (1.7)	*1*	17	59	23
benzodiazepine	4.7 (1.8)	*0*	20	49	32
fluvoxamine	4.7 (1.5)	*0*	12	66	22
tricyclic antidepressant	4.7 (1.3)	*0*	6	75	19
beta-blocker	4.4 (1.7)	*1*	10	63	27
carbamazepine	4.1 (1.5)	*0*	6	57	37
antihistamine	3.6 (1.9)	*3*	7	38	55
		%	%	%	%

* = *Treatment of Choice* = *No Consensus* *Note: 1st Line percentage includes Treatment of Choice percentage*

30 MEDICAL COMORBIDITY, SIDE EFFECTS, SPECIAL PROBLEMS. Please rate the appropriateness of using each medication for agitation in an elderly patient with dementia who has one of the following complications. Assume the problem is stable and not causing delirium. Give your highest ratings to the listed medications that combine safety with effectiveness in the given condition.

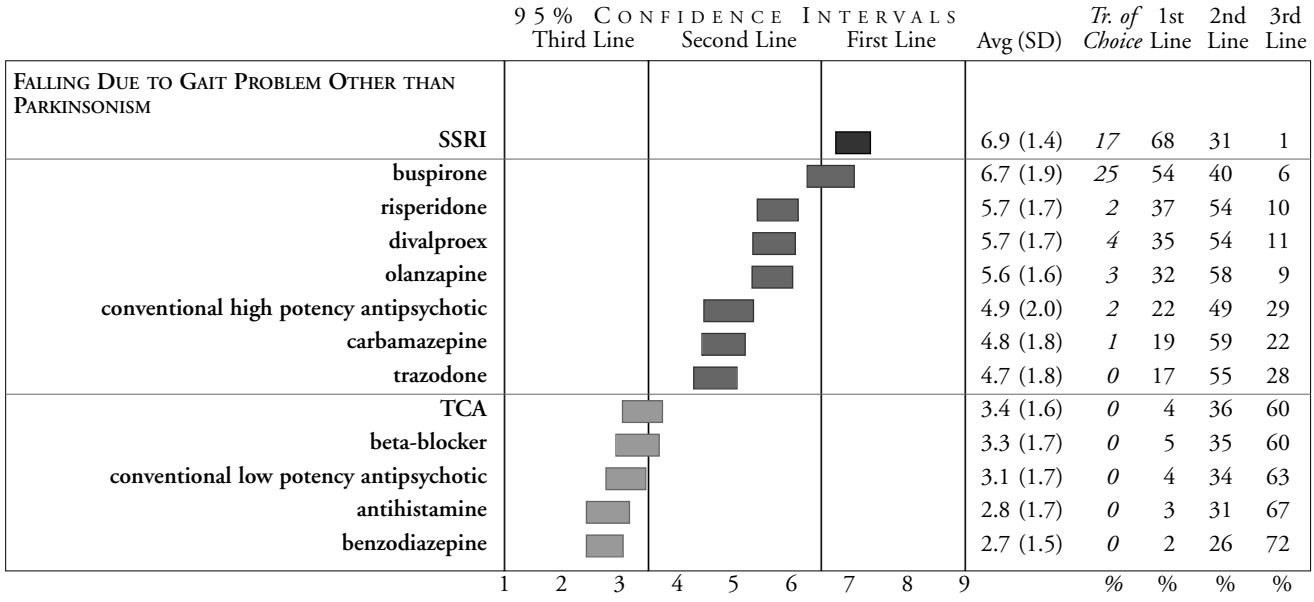
Comment:

Falling
Selective serotonin reuptake inhibitors (SSRIs) are the first line choice, followed closely by buspirone as the top second line choice. The experts recommend avoiding the third line options, which may cause falls as a result of orthostatic hypotension, coordination problems, or sedation.

Very poor memory
Fortunately, there are several medications that do not routinely cause marked memory impairment. Medications to be avoided are the tricyclic antidepressants (TCAs), conventional low potency antipsychotics, and benzodiazepines.

Nausea or poor appetite
Maintaining adequate nutrition and hydration can become a serious problem in some elderly patients. Antipsychotics receive the highest ratings because of their antiemetic effects. Clinicians should be alert to the fact that many other medications, in particular SSRIs, can occasionally cause nausea or impair appetite. These problems can often be minimized by beginning with low doses and titrating up slowly.

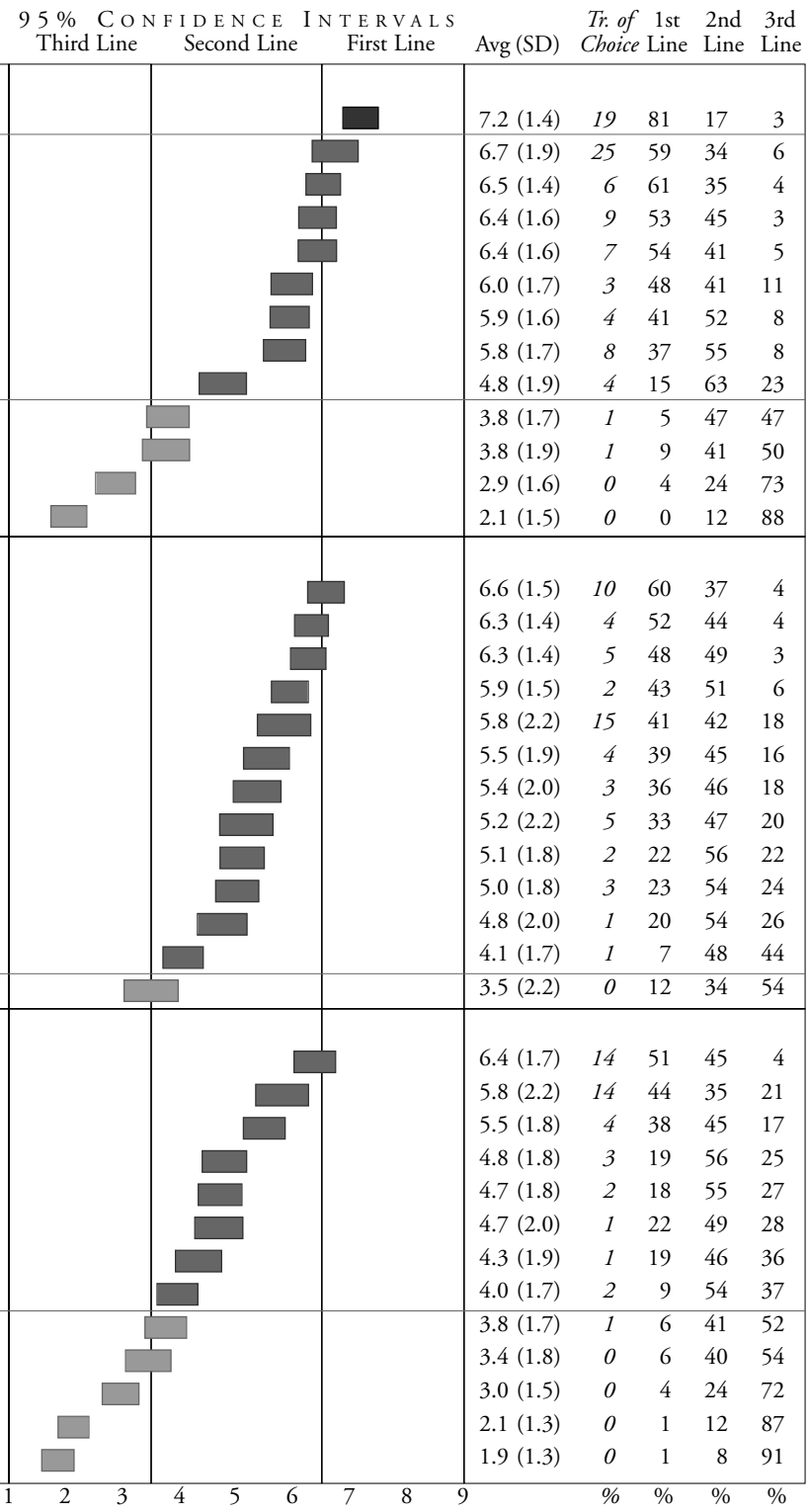
Lethargy
SSRIs, buspirone, and risperidone are less likely to exacerbate lethargy and may sometimes even be activating. Trazodone, conventional antipsychotics, and benzodiazepines are sedating and should therefore be avoided if lethargy is a problem. Note that, while medications vary in the degree to which they may cause lethargy, some patients may become sedated on any medication.



	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
FALLING DUE TO GAIT PROBLEM OTHER THAN PARKINSONISM					
SSRI	6.9 (1.4)	*17*	68	31	1
buspirone	6.7 (1.9)	*25*	54	40	6
risperidone	5.7 (1.7)	*2*	37	54	10
divalproex	5.7 (1.7)	*4*	35	54	11
olanzapine	5.6 (1.6)	*3*	32	58	9
conventional high potency antipsychotic	4.9 (2.0)	*2*	22	49	29
carbamazepine	4.8 (1.8)	*1*	19	59	22
trazodone	4.7 (1.8)	*0*	17	55	28
TCA	3.4 (1.6)	*0*	4	36	60
beta-blocker	3.3 (1.7)	*0*	5	35	60
conventional low potency antipsychotic	3.1 (1.7)	*0*	4	34	63
antihistamine	2.8 (1.7)	*0*	3	31	67
benzodiazepine	2.7 (1.5)	*0*	2	26	72
		%	%	%	%

* = *Treatment of Choice* ☐ = *No Consensus* *Note: 1st Line percentage includes Treatment of Choice percentage*

30 *continued*



	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
VERY POOR MEMORY					
SSRI	7.2 (1.4)	*19*	81	17	3
buspirone	6.7 (1.9)	*25*	59	34	6
risperidone	6.5 (1.4)	*6*	61	35	4
divalproex	6.4 (1.6)	*9*	53	45	3
conventional high potency antipsychotic	6.4 (1.6)	*7*	54	41	5
olanzapine	6.0 (1.7)	*3*	48	41	11
trazodone	5.9 (1.6)	*4*	41	52	8
carbamazepine	5.8 (1.7)	*8*	37	55	8
beta-blocker	4.8 (1.9)	*4*	15	63	23
TCA	3.8 (1.7)	*1*	5	47	47
conventional low potency antipsychotic	3.8 (1.9)	*1*	9	41	50
benzodiazepine	2.9 (1.6)	*0*	4	24	73
antihistamine	2.1 (1.5)	*0*	0	12	88
NAUSEA OR POOR APPETITE					
conventional high potency antipsychotic	6.6 (1.5)	*10*	60	37	4
risperidone	6.3 (1.4)	*4*	52	44	4
olanzapine	6.3 (1.4)	*5*	48	49	3
trazodone	5.9 (1.5)	*2*	43	51	6
buspirone	5.8 (2.2)	*15*	41	42	18
TCA	5.5 (1.9)	*4*	39	45	16
conventional low potency antipsychotic	5.4 (2.0)	*3*	36	46	18
benzodiazepine	5.2 (2.2)	*5*	33	47	20
divalproex	5.1 (1.8)	*2*	22	56	22
carbamazepine	5.0 (1.8)	*3*	23	54	24
beta-blocker	4.8 (2.0)	*1*	20	54	26
SSRI	4.1 (1.7)	*1*	7	48	44
antihistamine	3.5 (2.2)	*0*	12	34	54
LETHARGY					
SSRI	6.4 (1.7)	*14*	51	45	4
buspirone	5.8 (2.2)	*14*	44	35	21
risperidone	5.5 (1.8)	*4*	38	45	17
olanzapine	4.8 (1.8)	*3*	19	56	25
conventional high potency antipsychotic	4.7 (1.8)	*2*	18	55	27
divalproex	4.7 (2.0)	*1*	22	49	28
carbamazepine	4.3 (1.9)	*1*	19	46	36
TCA	4.0 (1.7)	*2*	9	54	37
trazodone	3.8 (1.7)	*1*	6	41	52
beta-blocker	3.4 (1.8)	*0*	6	40	54
conventional low potency antipsychotic	3.0 (1.5)	*0*	4	24	72
benzodiazepine	2.1 (1.3)	*0*	1	12	87
antihistamine	1.9 (1.3)	*0*	1	8	91
		%	%	%	%

* = *Treatment of Choice* ☐ = *No Consensus*

Note: 1st Line percentage includes Treatment of Choice percentage

31 MEDICAL COMORBIDITY, *continued*: Please rate the appropriateness of each medication for agitation in an elderly patient with dementia who has one of the following complications.

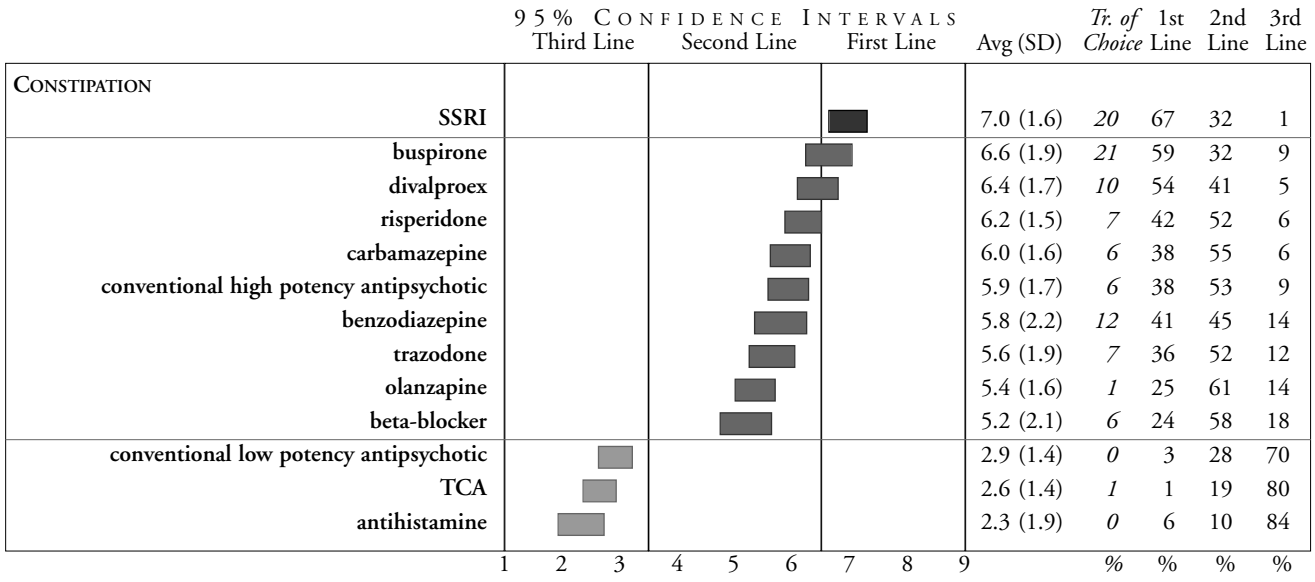
Comment:

Constipation
Selective serotonin reuptake inhibitors (SSRIs), buspirone, and divalproex, all of which lack significant anticholinergic properties, are least likely to exacerbate constipation and may even cause diarrhea. Medications with strong anticholinergic effects may exacerbate problems with constipation. If it is necessary to use these medications, the clinician should consider also giving a stool softener.

Concern over weight gain
SSRIs and buspirone are least likely to produce unwanted weight gain. Weight gain is a particular problem with the tricyclic antidepressants (TCAs) and conventional low potency antipsychotics. Many of the other medications listed sometimes cause unwanted weight gain in younger patients and are potentially a concern in the elderly.

Prostatic hypertrophy
SSRIs, buspirone, and divalproex, all of which lack significant anticholinergic properties, are least likely to exacerbate urinary retention associated with prostatic hypertrophy. Medications with strong anticholinergic effects are the most difficult to use in these patients.

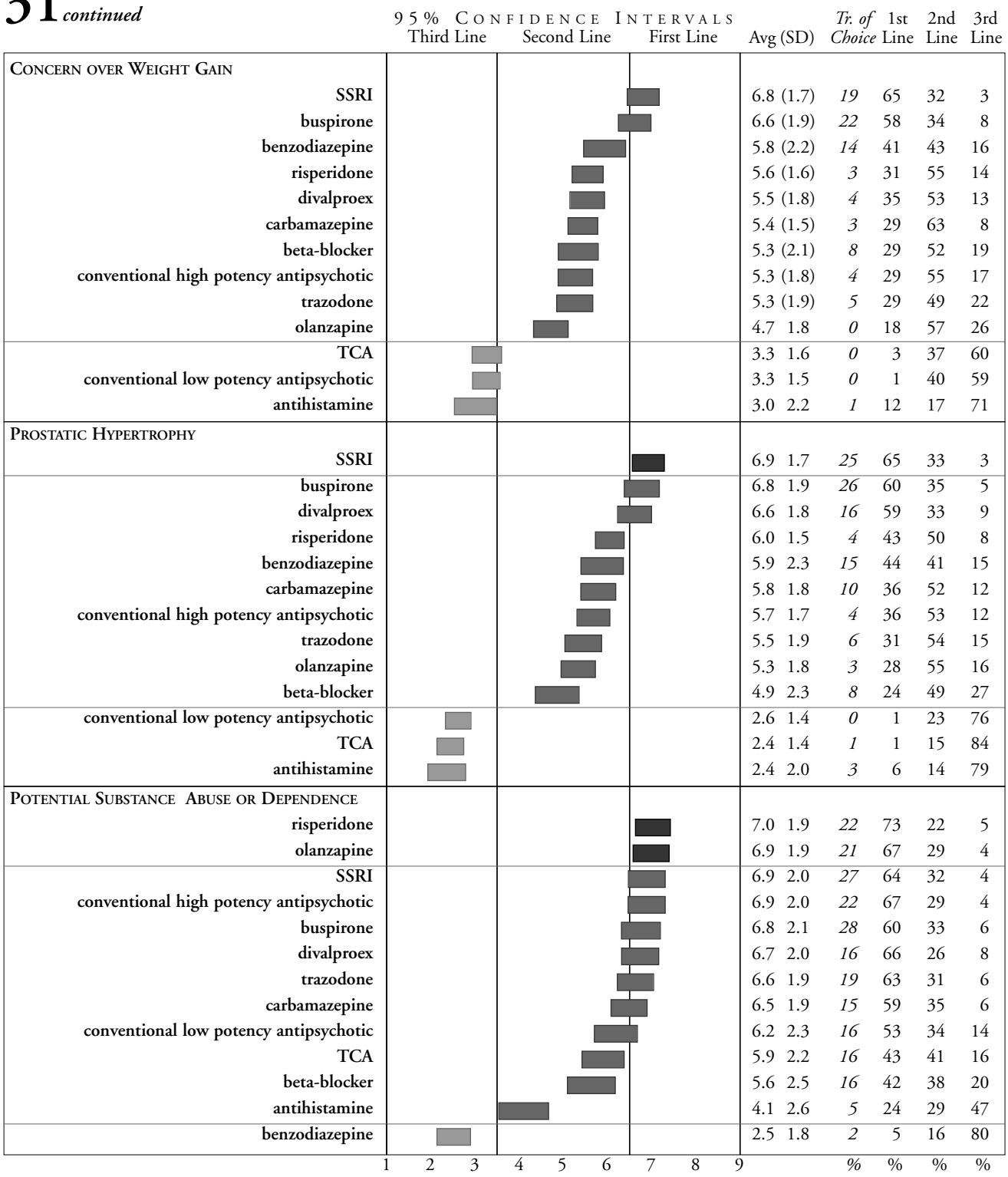
Potential substance abuse or dependence
All the medications listed have low abuse potential except for the benzodiazepines, which may also cause physiological dependence and severe withdrawal syndromes.



	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
CONSTIPATION					
SSRI	7.0 (1.6)	*20*	67	32	1
buspirone	6.6 (1.9)	*21*	59	32	9
divalproex	6.4 (1.7)	*10*	54	41	5
risperidone	6.2 (1.5)	*7*	42	52	6
carbamazepine	6.0 (1.6)	*6*	38	55	6
conventional high potency antipsychotic	5.9 (1.7)	*6*	38	53	9
benzodiazepine	5.8 (2.2)	*12*	41	45	14
trazodone	5.6 (1.9)	*7*	36	52	12
olanzapine	5.4 (1.6)	*1*	25	61	14
beta-blocker	5.2 (2.1)	*6*	24	58	18
conventional low potency antipsychotic	2.9 (1.4)	*0*	3	28	70
TCA	2.6 (1.4)	*1*	1	19	80
antihistamine	2.3 (1.9)	*0*	6	10	84
		%	%	%	%

* = *Treatment of Choice* ☐ = *No Consensus* *Note: 1st Line percentage includes Treatment of Choice percentage*

31 *continued*



	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
Concern over Weight Gain					
SSRI	6.8 (1.7)	*19*	65	32	3
buspirone	6.6 (1.9)	*22*	58	34	8
benzodiazepine	5.8 (2.2)	*14*	41	43	16
risperidone	5.6 (1.6)	*3*	31	55	14
divalproex	5.5 (1.8)	*4*	35	53	13
carbamazepine	5.4 (1.5)	*3*	29	63	8
beta-blocker	5.3 (2.1)	*8*	29	52	19
conventional high potency antipsychotic	5.3 (1.8)	*4*	29	55	17
trazodone	5.3 (1.9)	*5*	29	49	22
olanzapine	4.7 1.8	*0*	18	57	26
TCA	3.3 1.6	*0*	3	37	60
conventional low potency antipsychotic	3.3 1.5	*0*	1	40	59
antihistamine	3.0 2.2	*1*	12	17	71
Prostatic Hypertrophy					
SSRI	6.9 1.7	*25*	65	33	3
buspirone	6.8 1.9	*26*	60	35	5
divalproex	6.6 1.8	*16*	59	33	9
risperidone	6.0 1.5	*4*	43	50	8
benzodiazepine	5.9 2.3	*15*	44	41	15
carbamazepine	5.8 1.8	*10*	36	52	12
conventional high potency antipsychotic	5.7 1.7	*4*	36	53	12
trazodone	5.5 1.9	*6*	31	54	15
olanzapine	5.3 1.8	*3*	28	55	16
beta-blocker	4.9 2.3	*8*	24	49	27
conventional low potency antipsychotic	2.6 1.4	*0*	1	23	76
TCA	2.4 1.4	*1*	1	15	84
antihistamine	2.4 2.0	*3*	6	14	79
Potential Substance Abuse or Dependence					
risperidone	7.0 1.9	*22*	73	22	5
olanzapine	6.9 1.9	*21*	67	29	4
SSRI	6.9 2.0	*27*	64	32	4
conventional high potency antipsychotic	6.9 2.0	*22*	67	29	4
buspirone	6.8 2.1	*28*	60	33	6
divalproex	6.7 2.0	*16*	66	26	8
trazodone	6.6 1.9	*19*	63	31	6
carbamazepine	6.5 1.9	*15*	59	35	6
conventional low potency antipsychotic	6.2 2.3	*16*	53	34	14
TCA	5.9 2.2	*16*	43	41	16
beta-blocker	5.6 2.5	*16*	42	38	20
antihistamine	4.1 2.6	*5*	24	29	47
benzodiazepine	2.5 1.8	*2*	5	16	80
		%	%	%	%

* = *Treatment of Choice* = *No Consensus*

Note: 1st Line percentage includes Treatment of Choice percentage

32 MEDICAL COMORBIDITY, *continued*: Please rate the appropriateness of each medication for agitation in an elderly patient with dementia who has one of the following complications.

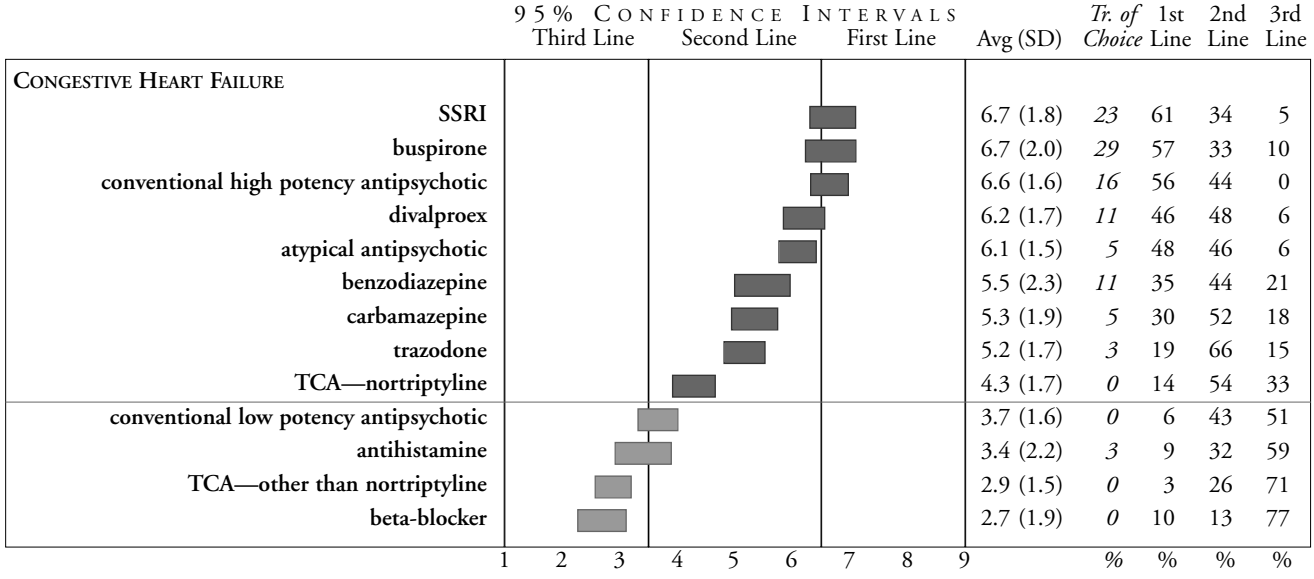
Comment:

Congestive heart failure
The experts are most comfortable with buspirone, the selective serotonin reuptake inhibitors (SSRIs), atypical and conventional high potency antipsychotics, and divalproex. They recommend avoiding conventional low potency antipsychotics and tricyclic antidepressants (TCAs) (even nortriptyline received a fairly low rating), probably because of the potential to exacerbate orthostatic hypotension and rhythm disturbances.

Orthostatic hypotension
The experts are most comfortable with the SSRIs, buspirone, atypical and conventional high potency antipsychotics, and divalproex. They recommend avoiding conventional low potency antipsychotics and TCAs. If one must use a TCA, nortriptyline would be preferable.

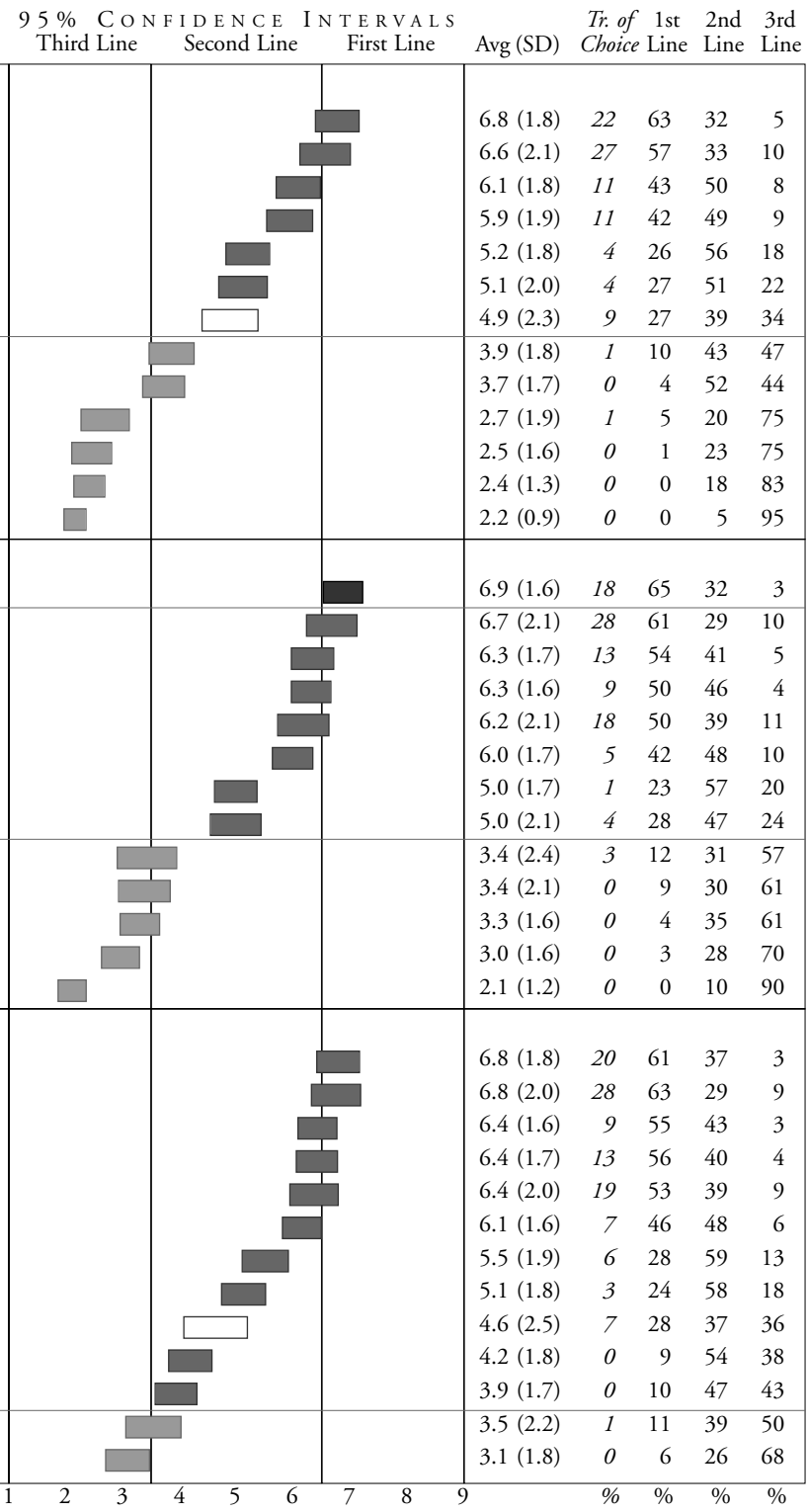
Cardiac conduction disease
The experts are most comfortable with the SSRIs, buspirone, divalproex, atypical and conventional high potency antipsychotics, and benzodiazepines. Benzodiazepines received a more favorable rating here than in the two previous situations because they may cause respiratory problems in patients with congestive heart failure or increase the likelihood of falling in patients with orthostatic hypotension. The experts recommend avoiding conventional low potency antipsychotics and TCAs. Note that the structure of carbamazepine resembles that of the TCAs and, like them, carbamazepine may exacerbate cardiac conduction disease.

Angina
The experts are most comfortable with the SSRIs, buspirone, divalproex, atypical and conventional high potency antipsychotics, and benzodiazepines. Benzodiazepines received a more favorable rating here, probably because they may be helpful in relieving acute anxiety in patients with chest pain. The experts recommend avoiding conventional low potency antipsychotics and TCAs other than nortriptyline.



* = *Treatment of Choice* = *No Consensus* *Note: 1st Line percentage includes Treatment of Choice percentage*

32 *continued*



	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
Orthostatic Hypotension					
SSRI	6.8 (1.8)	*22*	63	32	5
buspirone	6.6 (2.1)	*27*	57	33	10
conventional high potency antipsychotic	6.1 (1.8)	*11*	43	50	8
divalproex	5.9 (1.9)	*11*	42	49	9
atypical antipsychotic	5.2 (1.8)	*4*	26	56	18
carbamazepine	5.1 (2.0)	*4*	27	51	22
benzodiazepine	4.9 (2.3)	*9*	27	39	34
trazodone	3.9 (1.8)	*1*	10	43	47
TCA—nortriptyline	3.7 (1.7)	*0*	4	52	44
antihistamine	2.7 (1.9)	*1*	5	20	75
beta-blocker	2.5 (1.6)	*0*	1	23	75
conventional low potency antipsychotic	2.4 (1.3)	*0*	0	18	83
TCA—other than nortriptyline	2.2 (0.9)	*0*	0	5	95
Cardiac Conduction Disease					
SSRI	6.9 (1.6)	*18*	65	32	3
buspirone	6.7 (2.1)	*28*	61	29	10
divalproex	6.3 (1.7)	*13*	54	41	5
conventional high potency antipsychotic	6.3 (1.6)	*9*	50	46	4
benzodiazepine	6.2 (2.1)	*18*	50	39	11
atypical antipsychotic	6.0 (1.7)	*5*	42	48	10
trazodone	5.0 (1.7)	*1*	23	57	20
carbamazepine	5.0 (2.1)	*4*	28	47	24
antihistamine	3.4 (2.4)	*3*	12	31	57
beta-blocker	3.4 (2.1)	*0*	9	30	61
conventional low potency antipsychotic	3.3 (1.6)	*0*	4	35	61
TCA—nortriptyline	3.0 (1.6)	*0*	3	28	70
TCA—other than nortriptyline	2.1 (1.2)	*0*	0	10	90
Angina					
SSRI	6.8 (1.8)	*20*	61	37	3
buspirone	6.8 (2.0)	*28*	63	29	9
conventional high potency antipsychotic	6.4 (1.6)	*9*	55	43	3
divalproex	6.4 (1.7)	*13*	56	40	4
benzodiazepine	6.4 (2.0)	*19*	53	39	9
atypical antipsychotic	6.1 (1.6)	*7*	46	48	6
carbamazepine	5.5 (1.9)	*6*	28	59	13
trazodone	5.1 (1.8)	*3*	24	58	18
beta-blocker	4.6 (2.5)	*7*	28	37	36
TCA—nortriptyline	4.2 (1.8)	*0*	9	54	38
conventional low potency antipsychotic	3.9 (1.7)	*0*	10	47	43
antihistamine	3.5 (2.2)	*1*	11	39	50
TCA—other than nortriptyline	3.1 (1.8)	*0*	6	26	68
		%	%	%	%

* = *Treatment of Choice* ☐ = *No Consensus* *Note: 1st Line percentage includes Treatment of Choice percentage*

33 MEDICAL COMORBIDITY, *continued*: Please rate the appropriateness of each medication for agitation in an elderly patient with dementia who has one of the following complications.

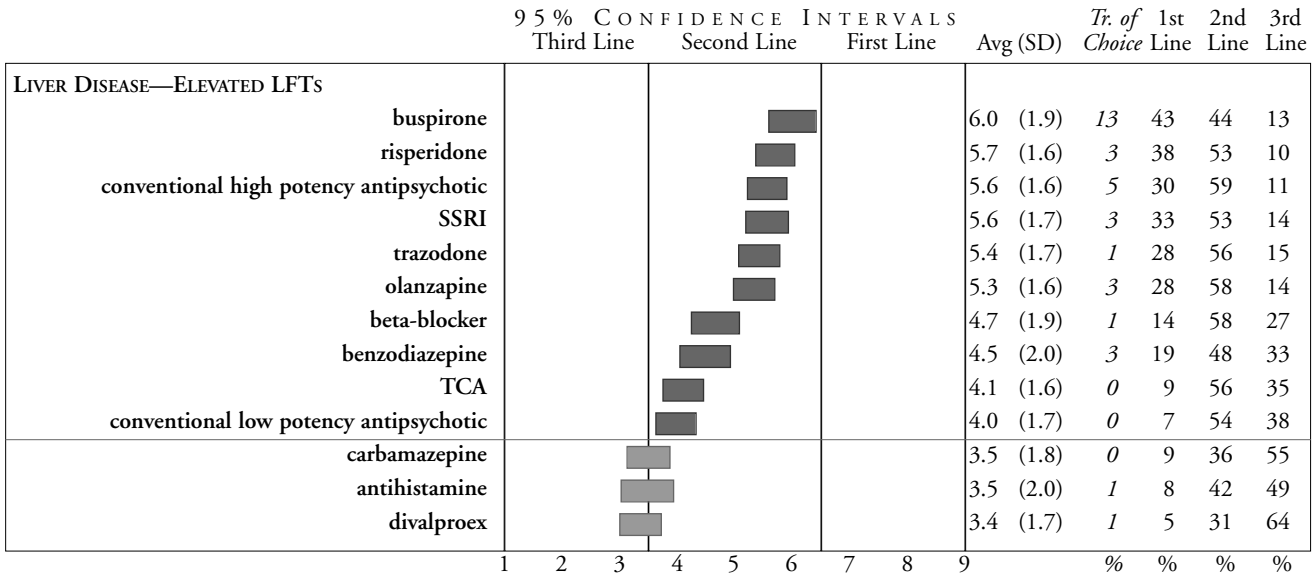
Comment:

Liver disease—elevated liver function tests (LFTs)
Conventional low potency antipsychotics, carbamazepine, and divalproex should be avoided in patients with liver disease because these medications are sometimes hepatotoxic. If a benzodiazepine must be used, clinicians should probably avoid those that are long-acting or have multiple active hepatic metabolites.

Renal insufficiency
Most drugs for agitation can be safely used in patients with renal problems provided lower doses are used and blood levels are monitored when possible. Although their clearance is relatively dependent on hepatic metabolism, a portion of each of these medications or their metabolites may be excreted through the kidneys.

Seizure disorder
Seizure disorder may be an independent problem predating the dementia, or seizures may develop late in life as a consequence of strokes or other dementing disorders. Divalproex is the treatment of choice for patients with dementia, agitation, and seizures, followed by carbamazepine. Other choices are reasonably safe, especially since an anticonvulsant will presumably be used for seizure control. Tricyclic antidepressants and conventional low potency antipsychotics are more likely than other medications to lower seizure thresholds; bupropion should be avoided in patients with seizure disorder.

Chronic obstructive pulmonary disease (COPD)
Most choices for agitation appear reasonable in patients with COPD, with the notable exceptions of benzodiazepines (which depress respiration) and beta-blockers (which may promote bronchospasm).



* = *Treatment of Choice* □ = *No Consensus* *Note: 1st Line percentage includes Treatment of Choice percentage*

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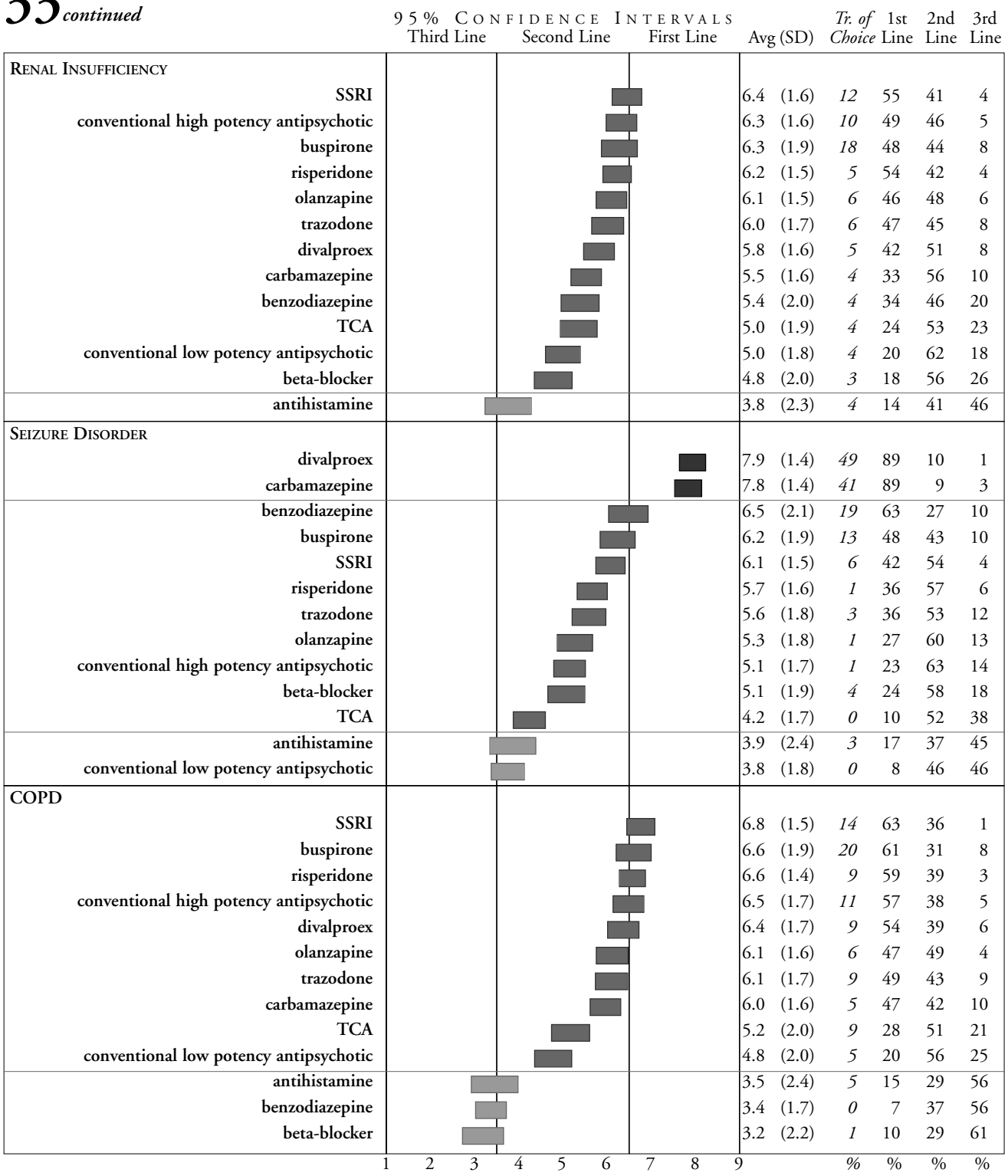

	Avg (SD)	*Tr. of Choice*	1st Line	2nd Line	3rd Line
Renal Insufficiency					
SSRI	6.4 (1.6)	*12*	55	41	4
conventional high potency antipsychotic	6.3 (1.6)	*10*	49	46	5
buspirone	6.3 (1.9)	*18*	48	44	8
risperidone	6.2 (1.5)	*5*	54	42	4
olanzapine	6.1 (1.5)	*6*	46	48	6
trazodone	6.0 (1.7)	*6*	47	45	8
divalproex	5.8 (1.6)	*5*	42	51	8
carbamazepine	5.5 (1.6)	*4*	33	56	10
benzodiazepine	5.4 (2.0)	*4*	34	46	20
TCA	5.0 (1.9)	*4*	24	53	23
conventional low potency antipsychotic	5.0 (1.8)	*4*	20	62	18
beta-blocker	4.8 (2.0)	*3*	18	56	26
antihistamine	3.8 (2.3)	*4*	14	41	46
Seizure Disorder					
divalproex	7.9 (1.4)	*49*	89	10	1
carbamazepine	7.8 (1.4)	*41*	89	9	3
benzodiazepine	6.5 (2.1)	*19*	63	27	10
buspirone	6.2 (1.9)	*13*	48	43	10
SSRI	6.1 (1.5)	*6*	42	54	4
risperidone	5.7 (1.6)	*1*	36	57	6
trazodone	5.6 (1.8)	*3*	36	53	12
olanzapine	5.3 (1.8)	*1*	27	60	13
conventional high potency antipsychotic	5.1 (1.7)	*1*	23	63	14
beta-blocker	5.1 (1.9)	*4*	24	58	18
TCA	4.2 (1.7)	*0*	10	52	38
antihistamine	3.9 (2.4)	*3*	17	37	45
conventional low potency antipsychotic	3.8 (1.8)	*0*	8	46	46
COPD					
SSRI	6.8 (1.5)	*14*	63	36	1
buspirone	6.6 (1.9)	*20*	61	31	8
risperidone	6.6 (1.4)	*9*	59	39	3
conventional high potency antipsychotic	6.5 (1.7)	*11*	57	38	5
divalproex	6.4 (1.7)	*9*	54	39	6
olanzapine	6.1 (1.6)	*6*	47	49	4
trazodone	6.1 (1.7)	*9*	49	43	9
carbamazepine	6.0 (1.6)	*5*	47	42	10
TCA	5.2 (2.0)	*9*	28	51	21
conventional low potency antipsychotic	4.8 (2.0)	*5*	20	56	25
antihistamine	3.5 (2.4)	*5*	15	29	56
benzodiazepine	3.4 (1.7)	*0*	7	37	56
beta-blocker	3.2 (2.2)	*1*	10	29	61
		%	%	%	%

* = *Treatment of Choice* ☐ = *No Consensus*

Note: 1st Line percentage includes Treatment of Choice percentage

Agitation in Older Persons with Dementia: A Guide for Families and Caregivers

If someone you care about has been diagnosed with dementia, you may feel that you are the only person facing the difficulties of this illness. But you are not alone. In the United States, more than 10% of the population over age 65 has dementia (more than 4 million Americans). As people in our society live longer and in better overall health, it is sad that many of us have to face the decline in memory and thinking of someone we love—we slowly seem to lose the person we knew even while life continues.

Living with someone who has dementia can be painful, confusing, and stressful. Although dementia is a disorder of memory, many people affected by it also develop agitation, which makes it much harder to care for them. Even under the best circumstances, families are often surprised by how angry or guilty they feel when they lose patience with their loved one.

But there is good reason to be optimistic. There are many things you can do to help your loved one and yourself. Support groups and national organizations offer practical advice that can help you solve problems and feel better about the job you are doing. You can learn about ways to go about daily routines and activities that help a person with dementia feel calmer and more secure, reducing his or her agitation. There are also medicines that can help. In this guide, we discuss these strategies for reducing agitation, which are based on the recent recommendations of a panel of expert doctors.

WHAT IS DEMENTIA?

The term *dementia* refers to a severe loss of thinking abilities, especially memory. It occurs most often in later years and is especially frequent in those over age 85. Some memory loss is normal as we age, but dementia is not. Many of us may worry that we are becoming "senile" if we become slightly forgetful or absent-minded, but these normal memory changes remain mild and do not impair our functioning. In contrast, dementia progresses to more and more serious problems, usually over several years. If you have any question, a doctor can help determine the difference for you.

Dementia is always caused by an underlying disease that damages brain tissue, leading to disturbed brain functioning. The most common such diseases are Alzheimer's disease and strokes (vascular disease). There are also less common causes, including Parkinson's disease, alcoholism, head injury, and others.

Alzheimer's disease causes gradual death of brain tissue due to biochemical problems inside individual brain cells. There is important research under way to determine the exact cause of the abnormality, which is not yet known. There are promising medicines that sometimes slow the pace of memory loss in Alzheimer's disease—we will not be discussing them in this guide, but you may want to ask your doctor about them. Researchers are working to find even better treatments as well as better tests to tell if someone has Alzheimer's disease, since it is often hard to make a clear diagnosis in the early stages. To learn more about these and other research advances, you can contact one of the organizations listed at the end of this guide.

A stroke occurs when a blood vessel in the brain is blocked or leaking. As a result, oxygen does not reach the area supplied by the blood vessel, and a section of the brain is damaged or dies (called an *infarct*). This causes a sudden loss of the functions performed by that section of the brain. Depending on its location, a stroke can cause loss of thinking abilities, of muscular control, or of sensation, or combinations of these. Dementia can result from a single large stroke, or the accumulated effect of many small strokes (*multi-infarct or vascular dementia*). Agitation after a stroke can be very severe. Stopping smoking and maintaining normal blood pressure and cholesterol levels all help prevent strokes. Medicines such as aspirin are also used to prevent some types of strokes. Your doctor will be familiar with these preventive approaches.

When an older person appears to have major changes in memory or thinking, a complete medical evaluation is essential. The evaluation determines if the problem has a temporary cause that can be easily reversed (such as an infection, a drug side effect, or a hormone deficiency) or if there is truly ongoing dementia from an underlying condition such as Alzheimer's disease or strokes. The doctor will perform a complete physical examination, including special neurological and memory tests, and will probably take blood tests. A specialized picture of the brain (such as a computed tomography [CT] scan or a magnetic resonance imaging [MRI] scan) is also sometimes taken.

WHAT IS AGITATION?

Many people with dementia experience emotional distress or behavioral changes best summed up by the term *agitation*. Very mild agitation may seem like a personality change in which a person acts in ways that are uncharacteristic or inappropriate for him or her, such as being very stubborn, worried, or nervous. More severe agitation forces caregivers to constantly supervise or reassure the person. These distressing symptoms can be disruptive or even dangerous. Agitation tends to persist and to grow worse over time, and severe agitation is often the reason that families eventually decide to place loved ones in nursing homes. Here are some behavioral problems you may encounter:

This guide was prepared by David Kahn, M.D., Lisa P. Gwyther, M.S.W., Allen Frances, M.D., Jonathan M. Silver, M.D., George Alexopoulos, M.D., and Ruth Ross, M.A. The authors thank the following organizations for their valuable help in reviewing this guide: The American Federation for Aging Research, the American Association for Retired Persons, and the National Citizens' Coalition for Nursing Home Reform. Abbott Laboratories, Bristol-Myers Squibb, and Janssen Pharmaceutica provided unrestricted educational grants in support of this project.

- Irritability, frustration, excessive anger
- "Blow-ups" out of all proportion to the cause
- Constant demands for attention and reassurance
- Repetitive questions, demands, or telephone calls
- Stubborn refusal to do things or go places
- Constant pacing, searching, rummaging
- Yelling, screaming, cursing, threats
- Hitting, biting, kicking

WHAT CAUSES AGITATION IN DEMENTIA?

We will discuss four problems that can cause agitation: physical and medical problems, environmental stresses, sleep problems, and psychiatric syndromes (psychosis, anger and aggression, depression, and anxiety). Remember that, in all these situations, a person with dementia is more easily agitated because the brain has physically changed and no longer functions in a healthy manner.

Physical and medical problems

If a person with dementia has recently become agitated for the first time or has a change from his or her usual behavior, the first thing to look for is a medical or physical problem.

Sudden illnesses may weaken the brain, causing worsened agitation. Your doctor might use the term *delirium* to describe an episode of agitation and confusion that begins suddenly because of a medical illness. Delirium improves when the medical problem gets better. The most common medical problems that can cause agitation or delirium are bladder infections, bad colds, bronchitis or pneumonia, and dehydration or poor nutrition (especially in people who forget to eat or can't feed themselves). It is also very important to make sure that someone who has become more agitated has not recently had a new stroke or been injured in a fall. Finally, flare-ups of chronic diseases such as diabetes or diseases of the heart, liver, or kidneys can cause agitation or delirium, especially if a person with dementia cannot take medications reliably or follow a special diet.

A toxic reaction to medication is an important cause of sudden confusion and agitation. Older people often take many different medications that can interact with each other. It is crucial to find out if side effects of a new prescription, interactions between medicines, or taking the wrong dose have led to a bad reaction.

Common physical problems that cause pain, discomfort, worry, or lack of sleep can lead to agitation by making the person upset or fatigued. Examples of such problems include arthritis, sitting all day in an uncomfortable position, constipation, and impaired vision or hearing.

Environmental stresses

People with dementia are very sensitive to the environment they live in. They are less able to handle changes, uncertainty, and other situations that they could manage when they were well. The ideal environment for a person with dementia provides clear, calm, comforting structure—often not an easy situation to arrange. Routine is very important, since changes in schedule or rushing can cause extreme disappointment, frustration, or fear. A physically comfortable environment is important. Noisy, poorly lit, or improperly heated areas can cause increased agitation. Extremes in the social environment can also cause problems (for example, if someone is left alone for long periods or is overwhelmed by being around too many people). Medical or dental procedures, and especially hospitalization, are particularly disruptive and can lead to sudden agitation or confusion in a person who was calm at home.

Sleep problems

Sleep problems are common in dementia. One type of problem is insomnia—trouble falling asleep at night or waking up throughout the night. Although the cause is often unclear, it is sometimes possible to pinpoint a reason that can be corrected, such as busy activities just before bedtime, using caffeine or alcohol, or drinking fluid before bedtime and then having to urinate. Conditions such as depression, nervousness, or physical pain can also cause insomnia. It also helps to keep in mind that many people need less sleep as they age, but that the person with dementia has a very hard time finding purposeful things to do during longer waking hours.

"Sundowning" is another type of sleep problem. Sleep patterns are controlled by an internal clock in our brain that senses day and night, telling us when to rest and when to be active. This clock is often damaged in dementia. The person may be awake and overactive at night, thinking it should be daytime and trying to get dressed and out of bed. This type of confusion, disorientation, and agitation is called sundowning because it usually begins in the early evening in a person who might otherwise be fairly clearheaded when awake during the daylight hours.

Psychiatric syndromes

Psychosis, aggression or anger, depression, and anxiety are common psychiatric syndromes seen in agitated persons suffering from dementia.

- **Psychosis** means being out of touch with reality in an irrational way. The person imagines things and is convinced these things are real. There are two types of psychotic symptoms: delusions (believing things that are not true) and hallucinations (hearing, seeing, or smelling things or feeling physical sensations on the skin that are not there). You cannot convince a person with psychosis that his or her beliefs are untrue. The most common delusions are believing that one is in danger from criminals, that others have stolen items or money, that a spouse is unfaithful, that unwelcome guests are living in the house, or that a relative is an imposter and not really the person he or she claims to be. These are also sometimes referred to as paranoid delusions and reflect fear and insecurity that result from being confused. Visual hallucinations such as seeing nonexistent visitors or burglars can cause a person to fearfully report events that have not actually occurred.
- **Anger and aggression.** Dementia causes the brain to lose its normal ability to control angry impulses, a problem called *disinhibition*. Anger becomes aggression when the person acts on these feelings by verbally or physically threatening another person or attacking objects. It may occur because the person with dementia often misunderstands or misinterprets the actions of others, and then lashes out because he or she feels ignored, in danger, or mistreated. Another cause of anger is frustration at being unable to complete tasks that were once easy, such as fixing something that

is broken, using the stove, or going to the bathroom. Sometimes there is no obvious cause of frustration. Anger and aggression can include verbal accusations and insults, aimless screaming, refusal to cooperate with requests to eat or bathe, and even physical assaults. Aggression can also include self-injury such as head banging or biting oneself. When a person with dementia becomes angry and aggressive, it is important to evaluate the person's environment to be sure it is safe and to see if some simple adjustments might reduce the problem. Although aggression is among the most distressing problems for caregivers, it can usually be helped with extra attention and sometimes medication; it should not be ignored in the hopes it will go away by itself.

- **Depression.** A person with depression feels sad or loses interest in things he or she normally enjoys. Although depression is an understandable reaction to an illness such as dementia, it is a treatable symptom, not a "normal" reaction, and should not be ignored. Successful treatment of depression helps individuals with dementia enjoy time with their families and other pleasurable activities. A diagnosis of depression should be considered if a person is often sad, tearful, or unable to enjoy anything or expresses constant thoughts of discouragement, failure, being a burden, or wanting to die or commit suicide. Depression often includes physical symptoms such as loss of appetite and weight, trouble sleeping, or complaints of physical pain. If no other medical cause is found for these physical symptoms, depression should be considered, even if the person denies feeling sad but just seems more withdrawn, apathetic, or disinterested. Agitation in depression can include extreme tearfulness, hand-wringing, an excessive need for reassurance, and other signs of extreme unhappiness. Depression can also cause delusions, most often guilty feelings about having done terrible things in the past.

- **Anxiety** means being very worried, overly fearful, nervous, fidgety, shaky, or frightened, either because of exaggerated fears or sometimes for no apparent reason. An important cause of anxiety may be the diagnosis of dementia itself, especially in the early stages when a person can feel embarrassed by making mistakes, forgetting things, or having trouble joining a conversation. An anxious person may not always be able to put the feelings into words, but instead may appear tense or have physical symptoms such as racing heart, nausea, or "butterflies in the stomach." Anxious people worry about things such as being alone, or they may fear that visitors will be late, that loved ones have been harmed, or that plans will be disrupted. They may become especially nervous when they are separated from caregivers, when schedules are changed, or when they are rushed or tired.

TREATMENT OF AGITATION

How soon should agitation be treated?

Agitation should be treated early, because it means the person with dementia is suffering emotionally or physically. Agitation doesn't go away by itself. Research studies show that it usually persists for 2 or more years, especially if it is associated with aggressive behavior. If treatment is begun early, there is an opportunity to find the most effective and safest treatment before agitation poses safety or health risks for the person or the family.

How is agitation treated?

There are a number of ways that you and the clinicians working with you can help an agitated person:

- **Providing the right environment**
- **Supervising activities**
- **Learning how to talk with a person who has dementia**
- **Getting support for families and caregivers and improving coping skills**
- **Medications**

PROVIDING THE RIGHT ENVIRONMENT

It is important to evaluate the person's environment—his or her bedroom, daytime areas, and schedule—to see if any of the following problems may be contributing to agitation:

- Some individuals become particularly agitated at specific times of the day. Would it help to change the person's routine to avoid these problems? It is helpful to try to do things in the same place at the same time each day.
- Agitation may result from thirst or hunger. If a person with dementia forgets to eat, offer frequent snacks and beverages.
- Agitation may result from physical discomfort. Has the person remembered to use the bathroom? Is he or she constipated? Could there be aches and pains from sitting in one place?
- Does the person have a regular, predictable routine? Unexpected changes or last-minute rushing can cause those with dementia to become scared and disoriented.
- Getting dressed can be frustrating for someone with dementia. Try to simplify this task, for example, by using Velcro fasteners and not insisting on matched outfits.
- Is there a chance for regular exercise? Walks and simple exercises are good ideas. If the person wants to pace and isn't disrupting anyone, that's OK too.
- Is the room well lighted? Good lighting can help reduce disorientation and confusion. Provide night-lights.
- Is the air temperature comfortable? Try to provide fresh air, heating, or air conditioning as needed.
- Is the environment too noisy or confusing? Are there too many people around? It may be helpful to use picture cues, to personalize the room, and to decorate and highlight important areas with bright, contrasting colors.
- Is the environment safe? If not, take the necessary steps to ensure the safety of the patient and caregiver (e.g., lock up knives and guns, take knobs off the stove at night, put safety latches on doors, camouflage unprotected exists, install inconspicuous locks to restrict access to cleaning solutions and other hazardous substances or poisons). It is a good idea to register the person with the SAFE RETURN program through the Alzheimer's Association in case he or she wanders off and gets lost.

SUPERVISING ACTIVITIES

People who are getting agitated can sometimes feel better if they have something useful or interesting to do. However, they usually need direction to find appropriate activities and to prevent frustration. Here are some suggestions that can help:

- **Structure and routine.** Try to follow regular, predictable routines that include pleasant, familiar activities. Remind the person that everything is going according to plan.
- **Pleasant activities.** Make time for simple pleasant activities the person knows and enjoys—listening to music, watching a movie or sporting event, sorting coins, playing simple card games, walking the dog, or dancing can all make a big difference.
- **Keep things simple.** Break down complex tasks into many small, simple steps that the person can handle (e.g., stirring a pot while dinner is being prepared; folding towels while doing the laundry). Allow time for frequent rests.
- **Redirect.** Sometimes the simplest way to deal with agitated behavior is to get the person to do something else as a substitute. For example, a person who is restless and fidgety can be asked to sweep, dust, rake, fold clothes, or take a walk with the caregiver. Someone who is rummaging can be given a collection of items to sort and arrange.
- **Distract.** Sometimes it is enough to offer a snack or put on a favorite videotape or some familiar music to interrupt behaviors that are becoming difficult.
- **Be flexible.** Your loved one might want to do some activity or behave in a way that at first troubles you, or may refuse to do something you have planned, like taking a bath. Before trying to interfere with a particular behavior, it is important to ask yourself if it is necessary to do so. Even if the behavior is bizarre, it may not be a problem, especially in the privacy of your own home.
- **Soothe.** When the person is agitated, it may help to do simple, repetitive activities such as massage, hair brushing, or giving a manicure.
- **Compensate.** Help the person with tasks that are too demanding. Don't put the person in a position where demands will be made that he or she cannot handle.
- **Reassure.** Let the person know that you are there and will keep him or her safe. Try to understand that fear and insecurity are the reasons the person may "shadow" you around and ask for constant reassurance.
- **Getting to doctor's appointments.** Is the person upset about going to the doctor or dentist? Here are some helpful hints: Emphasize the value of a checkup, rather than a test for a specific problem. Try to figure out if your relative is the type of person who does better with advance notice in order to prepare, or does better without being told ahead of time. Present the trip in a matter-of-fact manner as part of the day's plans. Allow enough time so that you are not rushed. If possible, have the relative or caregiver who works best with the patient come along to the appointment. If the person resists, don't argue; instead, try distractions like "We will go out to lunch afterward."

LEARNING HOW TO TALK WITH A PERSON WHO HAS DEMENTIA

People with dementia often find it hard to remember the meaning of words that you are using or to think of the words they want to say. You may both become frustrated. The following tips can help you communicate more effectively with a person who has dementia:

- It is understandable that you may feel angry; but showing your anger can make the agitation worse. If you are about to lose your temper, try "counting to ten," remembering that the person has a disease and is not deliberately trying to make things difficult for you.
- Try to talk about feelings rather than arguing over facts. For example, if the person with dementia is mistakenly convinced you didn't see him yesterday, focus on his or her feelings of insecurity today: "I won't forget you."
- Identify yourself by name and call the person by name. The person may not always remember who you are; don't ask, "Don't you remember me?"
- Approach the person slowly from the front and give him or her time to get used to your presence. Maintain eye contact. A gentle touch may help.
- Try to talk in a quiet place without too much background noise such as a television or other people in conversation.
- Speak slowly and distinctly. Use familiar words and short sentences.
- Keep things positive. Offer positive choices like "Let's go out now," or "Would you like to wear your red or blue cap?"
- If the person seems frustrated and you don't know what he or she wants, try to ask simple questions that can be answered with yes or no or one-word answers.
- Use gestures, visual cues, and verbal prompts to help. For example, if you suggest a walk, get out the coats, open the door, and say "Time for a walk." Set up needed supplies in advance for tasks such as bathing and getting dressed; have a special signal for needing to go to the bathroom. Try to break up complicated tasks into simple segments; physically start doing what you want to happen.
- If a subject of conversation makes a person more agitated or frustrated, it may help more if you drop the issue rather than keep on trying to correct a specific misunderstanding. He or she will probably forget the issue and be able to relax in a short while.

GETTING SUPPORT AND IMPROVING COPING SKILLS

Some of the behaviors that you see in your loved one may be very difficult, exhausting, and even frightening. When you feel frustrated, try to remember that these behaviors are part of the disease that has affected the person's brain. Many caregivers struggle with feelings of guilt and anger, and need support and reassurance to remember that the disease is creating the behavior, not the person they once knew.

Social support is important for caregivers, whose own mental health can be affected by the stress and sadness of helping someone with severe dementia and agitation. There are a number of sources of help, including organizations, newsletters, books, and computer sites

on the Internet—many of these are listed at the end of this guide. Joining a support group allows caregivers to meet and share ideas with others who are coping with similar problems. Group members who have "been there" can comfort you and often have good ideas for dealing with day-to-day problems. You can locate the nearest support group by contacting the Alzheimer's Association or sometimes community organizations such as a senior center or your local hospital.

Therapists can be helpful in dealing with stress, anxiety, or depression in family caregivers, and can help you sort out conflicts about priorities of time or living arrangements. Religious organizations can also help through support groups, and some individuals might find solace in counseling from a member of the clergy.

Sometimes caregivers find it very difficult to arrange time to attend educational meetings or groups outside the home. In this case, you might want to try one of the telephone helplines, most of which are toll-free. These offer trained peer counselors who are available to answer questions or just talk about problems you may be having. There are also a number of web sites, Internet chat groups, email listserves, and bulletin boards that can provide support and information for caregivers. In addition, there are many good educational publications and videotapes. Some have been written or produced by experts for families and caregivers; others have been written by family members or even individuals with dementia. At the end of this guide, we provide information on where to find all these resources.

MEDICATIONS

When are medications used to treat agitation?

Sometimes it is impossible to help a person become calm, despite your best efforts at providing warmth and structure. Medication for agitation can help you avoid caregiver "burnout" and make it easier for a suffering person to respond to your efforts. The more severe the agitation, the more important it is to consider medication. It does not "cure" dementia or agitation, but can reduce the frequency and severity of agitated behavior.

Doctors who are experts in geriatrics, psychiatry, or neurology are familiar with all of the medications we will be discussing. It is important to understand that most of the research in this area has been done with one group of medications (the antipsychotics, described more fully below). However, doctors often need to use other types of medicine. For this reason, the authors of this article conducted a survey to find out about the entire range of treatments that experts find helpful. Some trial-and-error is often involved before finding the right medication, dose, and schedule—every treatment plan is "custom-made." Although the doctor can help call the shots, it is a good idea for you to learn as much as you can about the various choices available in terms of their likely benefits and possible side effects. Ideally, you can become the doctor's partner, since you see the person more than anyone else and may be in the best position to know how a medication affects him or her.

Families sometimes fear that anti-agitation medicines will just sedate a person or make their confusion worse, or that they are shirking their responsibility by relying on medication. To the contrary, the careful use of medication can lessen agitation without unwanted sedation and make it more possible to care for and communicate with an ill person.

How are specific medications chosen for a person?

Experts choose different medications based on several factors:

- **Is the goal short-term or long-term?** The goal of short-term or acute treatment is to calm the person down quickly during a crisis. This often calls for sedation to make the person somewhat drowsy for a few hours. On the other hand, since agitation is often persistent, the goal may be to find a long-term treatment that can be used for many weeks or months without causing unwanted sedation or harmful side effects. However, it may take several weeks for such a treatment to begin working. This delay can require a fair amount of patience on the part of caregivers as doses are slowly and carefully adjusted.
- **What other medical problems does the person have, and what other medicines is he or she already taking?** General medical conditions cause a person to be more vulnerable to side effects of medications. Older people are often already taking several medicines, and it is extremely important to avoid interactions if another drug is added. Also, particular diseases may make it difficult to use certain anti-agitation medications. For example, people with lung disease should avoid medicines that might slow down their breathing, whereas those who fall or are unsteady on their feet should avoid medicines that might affect coordination.
- **What types of agitation symptoms does the person have?** In choosing a medication, it is also important to consider the types of agitation symptoms the person has. For example, some medicines might be best if the main problem is psychosis, whereas others would be more appropriate if the main problem is anxiety or depression.

What medication strategies are used for different types of agitation?

Many kinds of medication can be used to treat agitation, depending on the person's main symptoms. Doses are almost always lower than those used in younger persons, because our bodies eliminate drugs more slowly as we age and side effects are more likely. The experts' recommendations for broad treatment strategies are outlined in the Table on the next page. Each type of medicine is discussed in detail in the sections that follow.

Antipsychotics

Examples include:

- Conventional antipsychotics such as haloperidol (Haldol)
- Atypical antipsychotics such as risperidone (Risperdal), olanzapine (Zyprexa), and quetiapine (Seroquel); others are likely to be available in 1998.

Antipsychotic medications, also called neuroleptics, have been the mainstay for treating agitation for many years, both in clinical practice and in research studies. There are two kinds: *conventional antipsychotics*, which have been available for the past 40 years (11 conventional antipsychotics are on the market), and *atypical antipsychotics*, which have been widely used since the mid-1990s.

Antipsychotics are effective against delusions, hallucinations, aggression, and sundowning. They act rapidly and can be sedating, which makes them useful in emergencies. Haloperidol can also be given by injection if the need is urgent. Conventional antipsychotics

Medication Strategies

Main problem	Usual choices to start with
Delirium from a sudden medical problem	Conventional antipsychotic
Psychosis	Antipsychotic. For long-term use, an atypical antipsychotic is preferred.
Aggression, anger	Antipsychotic for short-term use
	Divalproex or antipsychotic for long-term use
Insomnia	Trazodone
	Benzodiazepines sometimes for short-term use only
"Sundowning" (confusion in late afternoon or early evening)	Trazodone
	Sometimes an antipsychotic
Anxiety	Buspirone for long-term use
	Benzodiazepine for short-term use only
Depression	Antidepressants, especially selective serotonin reuptake inhibitors
Pain from arthritis if over-the-counter pain medicines don't work	Tricyclic and other antidepressants

sometimes cause three kinds of neurological side effects: 1) muscle stiffness and tremor that resemble Parkinson's disease; 2) a restless feeling called akathisia that may make the person want to pace even more; and (3) after high doses given for many months or years, involuntary movements of the mouth or hands, a condition called tardive dyskinesia. A reasonable dose of haloperidol to treat agitation while minimizing side effects is about 1–2 mg/day, often given at bedtime.

The newer atypical antipsychotics represent a potential advance because they are less likely to cause neurological side effects. For this reason, many experts in our recent survey preferred to use atypical rather than conventional antipsychotics, especially for long-term treatment. Even though they cost more and are not always free of side effects, they may be preferable for many patients in the long run.

The atypical antipsychotics in widest use now are risperidone (Risperdal) and olanzapine (Zyprexa). Risperidone has been tested extensively in older patients with dementia and agitation. It can be as effective as conventional antipsychotics and, at a low dose, is usually free of neurological side effects. Possible side effects of risperidone are sedation and dizziness when standing. Side effects can be minimized by starting with a low dose, 1 mg or less per day. Small amounts can be given either by breaking a scored pill or using a liquid form. Olanzapine can be somewhat more sedating than risperidone, but is a useful alternative, especially for a person who has had muscle stiffness on risperidone, which occasionally happens, or for someone who has Parkinson's disease. The typical starting dose is a 2.5-mg pill at bedtime. Quetiapine (Seroquel) had just recently been introduced at the time we were writing this guide; other atypical antipsychotics are expected to be available soon and may prove useful as more is learned.

Antidepressants

The type of antidepressant most often recommended for older persons with dementia is a medication from the group known as selective serotonin reuptake inhibitors (SSRIs). Most experts prefer one of these two agents:

- sertraline (Zoloft)
- paroxetine (Paxil)

Other antidepressant choices to consider for an older person with dementia are listed below in alphabetical order:

- bupropion (Wellbutrin)
- desipramine (Norpramin, Pertofrane and others; a tricyclic)
- fluoxetine (Prozac, an SSRI)
- fluvoxamine (Luvox, an SSRI)
- nefazodone (Serzone)
- nortriptyline (Pamelor or Aventyl; a tricyclic)
- trazodone (Desyrel)
- venlafaxine (Effexor)

Clearly, there are many antidepressants to choose from. There is often a need to try several medications before finding the best one for an individual. It is important to be very patient, since it often takes several weeks to tell if a medicine is working. During the waiting period, you can sometimes help keep up a person's spirits with activities, a day program, or a support group.

Among the antidepressants, sertraline or paroxetine is often chosen first because these antidepressants have few side effects (occasionally insomnia or nausea) and are usually safe to combine with other medications an older person is likely to be taking, They are given once a day (usually in the morning). If these do not work, an alternative can be chosen, tailored to the needs of the individual. For example, bupropion and venlafaxine tend to be energizing and might be chosen for someone who is very withdrawn or apathetic. Nefazodone is relatively calming and might be a good choice for someone with a great deal of anxiety. The tricylic antidepressants tend to have more troublesome side effects, such as dry mouth, constipation, and dizziness if a person stands up too quickly. However, when used by experienced doctors and carefully monitored, they are sometimes quite effective in severe depression.

People with depression can also have delusions, such as a fear that body organs are not working, that they have been abandoned by everyone, or that they have no more money (when in fact they have). Delusional depression can be life-threatening due to suicide, or because of refusal to eat and drink, which can cause severe weight loss and dehydration. Agitation and trouble sleeping are also often very prominent. Although these symptoms can be very upsetting to witness, there are effective treatments. Usually, the first strategy is to combine the antidepressant with an antipsychotic medication. If severe depression or delusional depression does not respond to medications, electroconvulsive therapy can be lifesaving. Although there are many negative myths surrounding shock treatment, it is very safe

when given by experts and is an important tool for the severely depressed person who is in extreme suffering.

Antidepressants can also be used in conditions other than depression. Some antidepressants, especially the SSRIs, can help with anxiety. Tricyclics and SSRIs are also used for pain relief in arthritis and certain types of nerve pain if over-the-counter medicines like Tylenol or Advil haven't worked. Trazodone, a relative of nefazodone, is sold as an antidepressant but is usually too sedating for this purpose; we discuss it later as a sleeping aide.

Divalproex (Depakote)

Divalproex is best known as a treatment for brain disorders, such as epilepsy and seizures, and as a mood stabilizer for bipolar disorder (manic-depressive illness). It can also help with behavioral symptoms in older persons with dementia, especially in a person showing aggression, anger, or hypersexual behavior. It is often combined with an antipsychotic. The side effects of divalproex are nausea and sedation, which can usually be controlled by starting at small doses, making gradual adjustments, and monitoring the level of medication in the bloodstream. A low to average final dose of divalproex is 250 mg two or three times a day.

Carbamazepine (Tegretol)

Carbamazepine is another antiseizure medication that is also sometimes used for agitation. It can lower blood cell counts, which need to be monitored.

Buspirone (BuSpar)

Buspirone is an anti-anxiety medication that is not habit-forming and does not cause sedation. Buspirone is an excellent choice for someone who is very nervous or worried but does not have psychotic delusions. It is sometimes helpful for someone who gets angry too easily. It is also very safe to combine with other medications that an older person may be taking for general medical problems. Side effects of headache, dizziness, or nausea can occur if the dose is too strong; once in a while it can also cause overstimulation. Buspirone works gradually, and the dose usually needs to be adjusted over 2 to 6 weeks before beneficial effects can be judged. A typical starting dose is 5 to 7.5 mg twice a day, whereas a final dose may be 15 to 30 mg twice a day.

Trazodone (Desyrel)

Trazodone is a relatively safe, non-habit-forming medication that is technically considered to be an antidepressant, but is actually used more often simply to help the individual get a good night's sleep. It is also a good short-term alternative treatment for anxiety or when a mild sedative is needed. It should be started in very small amounts at first and adjusted upward until the right dose is found, usually about 50 mg. To help with sleep it should be given about 1 hour before bedtime. Its effects usually last about 8 hours, so if it is being used to help with daytime agitation, it may need to be given two or three times a day. Its main side effect is drowsiness if the dose is too high. Other side effects include dizziness when standing up and, very rarely, painful erections of the penis in men. Nefazodone (Serzone), a new antidepressant related to trazodone, is sometimes used for similar purposes; it may have fewer side effects.

Benzodiazepines

Examples include:

- lorazepam (Ativan)
- zolpidem (Ambien) (a related sedative)
- temazepam (Restoril)
- oxazepam (Serax)

Benzodiazepines are a group of about a dozen medications that cause sedation and can relieve anxiety. They are best used only in temporary situations—once in a while for sleep or for a daytime crisis of anxiety or agitation when someone needs to be calmed down quickly. In an emergency, benzodiazepines are sometimes combined with an antipsychotic; they can also be combined for a week or more with other medicines that may take longer to start working, such as divalproex.

The benzodiazepines listed above are preferred by experts for use in older people because they are cleared from the body relatively quickly. The effects of others, such as flurazepam (Dalmane) and clonazepam (Klonopin), can last 24 hours or longer; these longer-acting agents are usually best avoided because they may cause daytime sedation or falling. A typical dose of lorazepam is 0.5 mg; its effects last about 8 hours, so it is sometimes used two or three times over the course of a day for someone who is very agitated. Zolpidem, the effects of which last 6 to 8 hours, is usually given only to help sleep, at an average dose of 5 mg. Temazepam and oxazepam are good alternative choices that are cleared from the body relatively quickly. Benzodiazepines are habit-forming if used steadily for more than a few weeks; even single doses can cause unsteady gait and interfere with memory.

Because of the disadvantages of benzodiazepines, it is usually best to avoid using them for the long-term treatment of insomnia, anxiety, or agitation unless other choices have failed.

A FINAL WORD ABOUT AGITATION IN DEMENTIA

It is extremely painful to see a member of your family decline because of dementia, and especially difficult if agitation is also present. Remember that the behaviors are caused by a medical illness; that providing a calm, structured, safe, and caring environment can help; and that medications chosen carefully to address specific symptoms can alleviate distress and improve functioning. Research in treating agitation is only at the beginning. We have presented the best of current opinion, but much remains to be learned. The organizations listed below can help you find out about research studies of new treatments in which your loved one may be able to participate. Learn as much as you can about agitation and its treatment—your knowledge will make a difference in the quality of life for you and your affected family member.

RESOURCES

Nonprofit organizations and support groups

- Alzheimer's Association: 800-272-3900. The major self-help organization for people with Alzheimer's disease and their families. Over 200 local chapters sponsor support groups and seminars. Call for locations, and to find out about the telephone peer

helpline. Booklets and reading lists are available through the Green-Field Library: 312-335-9602.

- American Federation for Aging Research: 212-752-2327. A leading national organization supporting medical research on aging and age-related diseases to promote healthier aging. It publishes *Lifelong*, a monthly newsletter for patients and families.
- American Association of Retired Persons (AARP): 202-434-2277, 800-424-3410. Makes available booklets on specific topics such as *Coping and Caring*, *Nursing Home Life*, and *Staying at Home*.
- National Citizens' Coalition for Nursing Home Reform: 202-332-2275. Makes available booklets on getting the best care in nursing homes and about regulations that protect nursing home residents.
- Children of Aging Parents: 215-945-6900
- Help for Incontinent People: 864-579-7900, 800-BLADDER
- Insurance Consumer Helpline: 800-942-4242
- National Hospice Organization: 703-243-5900, 800-658-8898

Government agencies

- Alzheimer's Disease Education and Referral Center (ADEAR): 800-438-4380
- Eldercare Locator, for long-distance help finding services: 800-677-1116
- Medicare Hotline: 800-638-6833
- Social Security Information: 800-772-1213
- Agency for Health Care Policy and Research, Publications Clearing House (Request a free copy of *Early Alzheimer's Disease: Patient and Family Guide*): 800-358-9295

Readings and other educational materials (many available through the Alzheimer's Association or ADEAR)

Books written from the patient's perspective

Davis R. My journey into Alzheimer's disease. Wheaton, IL: Tyndale House; 1989

Rose L. Show me the way to go home. Forest Knolls, CA: Elder Books; 1996

Henderson CS. Musings. Durham, NC: The caregiver—Newsletter of the Duke Family Support Program; Fall 1992. Reprints are available from Box 3600, DUMC, Durham, NC 27710.

Books written by and for caregivers

Doernberg M. Stolen mind. Chapel Hill, NC: Algonquin Press; 1989 (out of print; check your local library)

Dyer L. In a tangled wood: an Alzheimer's journey. College Station, TX: Texas A&M University Press, 1996 (Call 800-826-8911)

Mace NL, Rabins PV. The thirty-six hour day: a family guide to caring for persons with Alzheimer's disease, related dementing illness, and memory loss in later life. 2nd revised ed. New York: Warner Books; 1992

National Institute on Aging. Talking with your doctor: a guide for older people. National Institutes of Health Publication No. 94-3452. (Call 800-222-2225 for a free copy)

Shanks L. Your name is Hughes Hannibal Shanks: a caregiver's guide to Alzheimer's disease. Lincoln, NE: University of Nebraska Press, 1996 (Call 800-755-1105)

Starkman EM. Learning to sit in silence: a journal of caretaking. Watsonville, CA: Papier-Mache Press; 1993

Videotapes

Alzheimer's Disease Caregiver's Kit. (Available from the Alzheimer's Association chapters or ADEAR)

Alzheimer's Disease, from Time-Life Medical. Narrated by C. Everett Koop, M.D. (Available at pharmacies and other stores)

Newsletters

Alzheimer's Association: National and local chapter newsletters

American Federation for Aging Research: *Lifelong* (monthly)

Parent care advisor. Monthly newsletter from LRP Publications, 747 Dresher Rd., PO Box 980, Horsham, PA 19044-0980

Wiser now. Monthly newsletter for Alzheimer's caregivers from Better Directions, PO Box 35, Spencerville, MD 20868-0055 (800-999-0795)

Computer Program

Living with Alzheimer's disease: help for caregivers of people with Alzheimer's Disease. An interactive computer program developed by the University of Wisconsin Center for Health Systems Research. Ask your healthcare provider to call 608-263-0492 for information.

Resources on the Internet

ADEAR web page: http://www.alzheimers.org

Alzheimer's Association web page: http://www.alz.org

Agency for Health Care Policy and Research web page: http://www.ahcpr.gov/clinic/alzcons.htm

Northern Virginia Alzheimer's Association web page, with excellent practical advice for families: http://www.alz-nova.org

E-mail support group: Send an e-mail message to: majordomo@wubios.wustl.edu. Write nothing in the subject line, but send a one-line message saying "subscribe alzheimer" (spelled just like that).

SAFE RETURN

To register a person in case he or she gets lost outside the home, call the Alzheimer's Association for an application: 800-272-3900; or write to SAFE RETURN, PO Box 9307, St. Louis, MO 63117-0307. There is a one-time $25 fee for registration. To report a lost person, call 800-572-1122.

FOR MORE INFORMATION PLEASE CONTACT US:

The recommendations in this article were based on a recent survey of experts in geriatric psychiatry (published as A Special Report to *Postgraduate Medicine*, March, 1998). You can learn more about this study, download the article for caregivers that you just read, or request reprints by contacting our website at:

www.psychguides.com

or by writing to us at:

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