

Documentation of Antipsychotic Use and Indications for Newly Diagnosed, Nonaggressive Dementia Patients

Nikhil Dhawan, B.A.; Avila B. Steele, Ph.D.; Robert O. Morgan, Ph.D.;
A. Lynn Snow, Ph.D.; Jessica A. Davila, Ph.D.; and Mark E. Kunik, M.D., M.P.H.

Objective: The purpose of this study was to determine the prevalence of antipsychotic use among nonaggressive patients with newly diagnosed dementia and to examine indications for antipsychotic use.

Method: Patients had to be veterans older than 60 years, newly diagnosed with dementia (ICD-9-CM criteria) from 2001 to 2004 at the Michael A. DeBakey Veterans Affairs Medical Center in Houston, Tex. Patients diagnosed more than 1 year before telephone screening, living in a nursing home or having a caregiver less than 8 hours a week, and/or having aggression, determined by caregiver response on the Ryden Aggression Scale, were excluded. Medical records of eligible participants were then evaluated on the basis of 5 questions: (1) Was the patient taking an antipsychotic? (2) Were neuropsychiatric symptoms documented, with or without antipsychotics? (3) Did the patient have comorbid psychiatric diagnoses? (4) Did the physician attempt to decrease or discontinue the antipsychotic? and (5) Did the physician attempt nonpharmacologic interventions?

Results: A total of 173 patients were eligible for medical record evaluation. Of these, 29 (17%) had been prescribed antipsychotics. Depression, nighttime disturbance, and irritability were the most often documented neuropsychiatric symptoms; however, 31% of patients had no documented symptoms. Mood disorder was documented in 36% of patient records; however, 94 patients (54%) had no comorbid psychiatric disorder. Twelve nonpharmacologic interventions were documented for dementia symptoms. Only 2 attempts to discontinue or decrease antipsychotics for the 29 patients using them were documented.

Conclusion: A sizable minority of newly diagnosed, nonaggressive dementia patients are taking antipsychotics. Physicians need greater education and awareness of the benefits of nonpharmacologic interventions.

(*Prim Care Companion J Clin Psychiatry* 2008;10:97-102)

Received Aug. 2, 2007; accepted Oct. 15, 2007. From the Houston Center for Quality of Care and Utilization Studies, Health Services Research (Mr. Dhawan and Drs. Steele, Morgan, Davila, and Kunik); the Department of Medicine, Baylor College of Medicine (Mr. Dhawan and Dr. Kunik); the Michael E. DeBakey Veterans Affairs (VA) Medical Center (Drs. Steele, Morgan, Davila, and Kunik); the Menninger Department of Psychiatry and Behavioral Sciences, Baylor College of Medicine (Drs. Steele and Kunik), Houston, Tex.; the Center for Mental Health and Aging, Department of Psychology, University of Alabama, and Tuscaloosa VA Medical Center, Tuscaloosa (Dr. Snow); and the VA South Central Mental Illness Research, Education, and Clinical Center (Dr. Kunik).

This study was conducted at the Michael A. DeBakey VA Medical Center in Houston, Tex., and was supported by Grant No. IIR 01-159-2 from the Department of Veterans Affairs, Veterans Health Administration, Health Services Research and Development Service, Washington, D.C. The study sponsors had no role in the design, conduct, analysis, interpretation, writing, or decision to publish this study.

The authors thank Annette Walder, M.S., for assistance with data analysis and Sonora Hudson, M.A., for editorial assistance during the preparation of this manuscript. Both Ms. Walder and Ms. Hudson are full-time VA employees of the Houston Center for Quality of Care and Utilization Studies. Neither has any conflict of interest to disclose.

The views expressed in this article are those of the authors and do not necessarily reflect the opinions of the Department of Veterans Affairs.

Mr. Dhawan received a Medical Student Training in Aging Research Grant from the American Federation of Aging Research. The authors report no additional financial or other relationships relevant to the subject of this article.

Corresponding author and reprints: Mark E. Kunik, M.D., M.P.H., Houston Center for Quality of Care and Utilization Studies, Michael A. DeBakey VAMC (152), 2002 Holcombe, Houston, TX 77030 (e-mail: mkunik@bcm.tmc.edu).

Over 4 million people have dementia, and estimates are that this number will continue to grow.¹ Ninety percent of patients with dementia display behavioral and psychological symptoms, such as agitation, wandering, depression, and anxiety. These symptoms increase the cost of care, caregiver burden, and risk of nursing home placement, and decrease patient quality of life.²⁻⁴ To care for dementia patients, clinicians must give as much if not more attention to managing associated behavioral problems as they do to attempting to slow the progression of cognitive decline.

Guidelines suggest that nonpharmacologic treatment, such as modification of daily activities or sensory therapy, should be first-line treatment for any behavioral and psychological symptom of dementia (BPSD).⁵⁻⁸ However, in practice there has been low adherence to using nonpharmacologic treatment.⁹ A reported 27% of dementia outpatients are taking antipsychotics,¹⁰ while one multicenter study found 32.4% antipsychotic use in nursing home

patients.¹¹ Furthermore, studies show a large variation in the prescribing practice of physicians.¹¹ According to guidelines, physicians should prescribe an antipsychotic for a BPSD only if first-line treatment fails and the symptom is distressing to the patient or caregiver, functionally disabling, preventing essential care, or endangering to self or others.⁵⁻⁸

Although most guidelines suggest the use of antipsychotics as an intervention for BPSDs, several recent controlled trials and meta-analyses fail to show a separation of the placebo response from the antipsychotic response for BPSDs.^{12,13} However, patients treated with antipsychotics do show more adverse effects of these drugs, including edema, extrapyramidal symptoms, abnormal gait, somnolence, cardiovascular accidents, urinary incontinence, and death. These recent findings indicate the potential ineffectiveness of antipsychotics in treating BPSD in dementia patients, while highlighting the increased mortality and disability associated with using this class of psychotropic in elderly patients. In 2005 the U.S. Food and Drug Administration placed a black box warning on antipsychotic agents regarding their use in elderly patients because of an increased risk of stroke and death.¹⁴ Despite this warning, some physicians continue to prescribe antipsychotics, arguing that they have a role in treating behavioral symptoms in dementia patients.¹⁵

To our knowledge, no study has looked at the pharmacologic interventions for BPSDs that physicians use in treating patients with newly diagnosed dementia without aggression. It is generally believed that early, newly diagnosed patients display fewer BPSDs. With this in mind, among a cohort of newly diagnosed, nonaggressive dementia patients, one would expect a low use of antipsychotics. Given new data on the low efficacy and substantial morbidity of antipsychotics, understanding the prevalence and reasons for antipsychotic use in this sample of patients will help guide interventions at the clinical and policy levels. Therefore, the purpose of this study was to determine the prevalence of antipsychotic use among patients with newly diagnosed dementia without aggression and to examine indications for antipsychotic use.

METHOD

Subjects

Newly diagnosed, nonaggressive dementia patients were initially identified through several sources (e.g., Veterans Administration Outpatient Data Files, flyers, and radio and print advertisements). To be included, patients had to be veterans, over 60 years of age, and newly diagnosed with dementia from 2001 to 2004 at the Michael E. DeBakey Veterans Affairs Medical Center in Houston, Texas. *Newly diagnosed* was defined as receiving an initial outpatient *International Classification of Diseases,*

Ninth Revision, Clinical Modification (ICD-9-CM) code for dementia (code 290.xx, 291.2, 292.82, 294.1, 294.8, or 331.0) in the 12 months before screening.

After determining eligibility, a research staff person sent a letter of notification to subjects stating that they would be contacted unless they called to decline to participate. Participants meeting the above criteria were screened by telephone to verify their eligibility. Patients were excluded if they had received a dementia diagnosis more than 1 year before the telephone screening, lived in a nursing home, or had a caregiver less than 8 hours per week. All dementia diagnoses were both formally confirmed through medical records and informally confirmed through caregiver report.

Presence of aggression was also an exclusion criterion. The patient was classified as aggressive if the caregiver responded positively to 1 or more items from the Ryden Aggression Scale.¹⁶ The Ryden Aggression Scale inquires about physical, verbal, and sexually aggressive behaviors during the previous year.

This research project was approved by the Houston Veterans Affairs Research Committee and the Baylor College of Medicine Institutional Review Board.

Medical Record Review

PubMed was searched in November 2006 using the following terms: *dementia, neuropsychiatric, agitation, BPSD, and antipsychotic*. From the results of these searches, relevant articles were reviewed to aid in creating a chart-abstraction tool to explore the following questions to examine prevalence, reasons for antipsychotic use, and adherence to practice guidelines. The specific questions addressed were: (1) Was the patient taking an antipsychotic? (2) Were any neuropsychiatric symptoms documented in patients with or without antipsychotics? (3) Did the patient with and without antipsychotics have any comorbid psychiatric diagnoses? (4) Did the physician attempt a trial of a decreased antipsychotic dose or discontinuation of the antipsychotic? (5) Did the physician attempt any nonpharmacologic interventions for BPSD?

A medical student trained and supervised by a board-certified geropsychiatrist completed the medical record review. The chart-abstraction tool was completed for each participant by reviewing the notes from 5 care areas (primary care, neurology, emergency, mental health, and social work) for 1 year before each patient's telephone-screening date. *Insufficient documentation* was defined as having less than 2 notes during the 12 months before study entry. In cases in which clarification was needed or documentation was ambiguous, notes from 2 additional care areas (pharmacy and nursing) were reviewed. For example, if in a neurology note a neurologist wrote "start inpatient Seroquel" without a supporting rationale or reason, then nursing care and pharmacy notes for that

particular patient were reviewed for clarification. In cases in which no clarification or support was found, then that particular chart was reviewed by the supervising geropsychiatrist.

Presence of an antipsychotic. The first question, “Was the patient taking an antipsychotic?” was answered by documenting all instances of patient prescriptions for antipsychotic medication. Medications that were prescribed on an as-needed basis, for either an inpatient stay or outpatient visit, were ignored.

Presence of documented neuropsychiatric symptoms. The second question attempted to explore the reason why a patient was prescribed an antipsychotic medication. “Were any neuropsychiatric symptoms documented?” was coded positive if that symptom was mentioned anywhere in primary care, neurology, emergency room, mental health, or social work notes 1 year before the screening date. The Neuropsychiatric Inventory Questionnaire (NPI-Q)^{17,18} was used to define the neuropsychiatric symptoms. For example, if the medical record stated “has trouble sleeping at night,” the NPI-Q symptom “nighttime disturbance” was coded. In other attempts to document neuropsychiatric symptoms, some patients (all nonaggressive at the time of initial screening) coded positive for agitation. During the review, if agitation was coded positive, a more in-depth exploration for aggression was performed. Aggression, as a neuropsychiatric symptom, was coded positive if there was clear documentation of verbal or physical aggression.

Presence of comorbid psychiatric disorders. Psychiatric diagnoses were categorized as mood, anxiety, or psychotic/thought disorders. Patient psychiatric symptoms were coded into neuropsychiatric symptoms based on symptoms listed in the NPI-Q scale. For example, a patient complaint of feeling depressed (e.g., “I am depressed”) was not enough to code positive for a mood disorder. Further, if a patient had a mood disorder with depression as part of the syndrome, this would not mean that he/she would code positive for depression in the neuropsychiatric scale. For example, one could have a past medical history of depression but could be in remission secondary to pharmacologic treatment and therefore not have depressed mood.

Attempts to decrease or discontinue antipsychotic. The medical records of all patients taking antipsychotics within the chart-abstraction period were searched for changes and discontinuation of their antipsychotic medication.

Documentation of nonpharmacologic interventions. The final question, “Did the physician attempt a nonpharmacologic intervention for a symptom of dementia?” was answered by documenting all instances of documentation of a symptom of dementia and developing a plan to treat this symptom. An example of this includes discussing the importance of not sleeping during the day to avoid insomnia and nighttime wandering.

Statistical Analyses

Frequency analyses were calculated to determine the proportions of dementia patients who were documented as having an antipsychotic prescription, neuropsychiatric symptoms, comorbid psychiatric disorders, nonpharmacologic interventions, and attempts to decrease or discontinue antipsychotic medications. Fisher exact tests were calculated to compare differences in antipsychotic use across comorbid psychiatric conditions. Statistical Analysis Systems software v.9.1 (SAS Institute, Inc., Cary, N.C.) was used for all analyses.

RESULTS

Of 217 medical records abstracted, 44 were excluded for insufficient documentation, leaving 173 nonaggressive, newly diagnosed dementia patients (172 men [99%] and 1 woman [1%]). Of the 173 patients, 145 (84%) were married, and 28 (16%) were widowed, divorced, or never married. Mean age of participants was 76 (SD = 5.89) years, with a range of 60 to 90 years. The ethnic background of participants was as follows: 126 (73%) white, 39 (23%) black, 7 (4%) Hispanic, and 1 (1%) American Indian/Alaskan Native. Of the 173 charts, 34 (20%) were reviewed by the geropsychiatrist for clarification and consensus.

Presence of an Antipsychotic

Twenty-nine patients (17%) were taking antipsychotics. Twelve of these (41%) had been prescribed the antipsychotic more than 1 year before the telephone-screening date, while 17 patients (59%) had been prescribed an antipsychotic during the 12 months before study entry. The most commonly prescribed antipsychotic was risperidone (N = 16, 55%). Others prescribed included quetiapine (N = 14, 48%), olanzapine (N = 4, 14%), mesoridazine (N = 1, 3%), and haloperidol (N = 1, 3%). Because a patient could be prescribed multiple antipsychotics during the chart-review period, either at the same time or at different times, the sum of the numbers of patients taking individual antipsychotics does not equal 29.

Presence of Neuropsychiatric Symptoms

The distribution of documented neuropsychiatric symptoms is shown in Table 1. Depression (N = 70, 40%), nighttime disturbance (N = 53, 31%), and irritability (N = 46, 27%) were the most common symptoms documented. No documented neuropsychiatric symptoms were found in 31% of the patient charts. Of the 53 patients with no documented psychiatric symptoms, 7% (N = 2) had been prescribed antipsychotic medication.

Presence of Comorbid Psychiatric Disorders

Mood disorder (N = 62, 36%) was the most common diagnosis documented, followed by anxiety disorder

Table 1. Documentation of Neuropsychiatric Symptoms in Newly Diagnosed, Nonaggressive Dementia Patients Within 1 Year of Screening^a

Symptom	On Antipsychotic Treatment (N = 29), N (%)	Not on Antipsychotic Treatment (N = 144), N (%)	Total (N = 173), N (%)	p Value
No symptoms documented	2 (7)	51 (35)	53 (31)	< .001
Depression	17 (59)	53 (37)	70 (40)	.06
Nighttime disturbances	15 (52)	38 (26)	53 (31)	< .05
Irritability	10 (34)	36 (25)	46 (27)	.18
Anxiety	10 (34)	29 (20)	39 (23)	.15
Hallucinations	13 (45)	8 (6)	21 (12)	< .001
Agitation	11 (38)	6 (4)	17 (10)	< .001
Appetite	6 (21)	8 (6)	14 (8)	< .05
Apathy	5 (17)	8 (6)	13 (8)	.05
Aberrant motor behavior	5 (17)	7 (5)	12 (7)	< .05
Delusions	8 (28)	4 (3)	12 (7)	< .001
Disinhibition	3 (10)	2 (1)	5 (3)	< .05
Euphoria	0 (0)	1 (1)	1 (1)	> .99

^aAnalyses: independent 2 × 2 tables using Fisher exact tests.

Table 2. Antipsychotic Use in Dementia Patients With Comorbid Psychiatric Conditions^a

Condition	On Antipsychotic Treatment (N = 29), N (%)	Not on Antipsychotic Treatment (N = 144), N (%)	Total, ^b (N = 173), N (%)	p Value
Mood disorder	12 (41)	50 (35)	62 (36)	.83
Anxiety disorder	4 (14)	14 (10)	18 (10)	.10
Thought disorder	7 (24)	2 (1)	9 (5)	< .001
Other disorder ^c	0 (0)	2 (1)	2 (1)	> .99
No psychiatric disorder	10 (34)	84 (58)	94 (54)	< .05

^aAnalyses: independent 2 × 2 tables using Fisher exact tests.

^bTotal percentages above 100% due to dual diagnoses.

^c“Other disorder” category includes adjustment disorder with depressed mood and a nightmare disorder.

(N = 18, 10%), thought disorder (N = 9, 5%), and other disorder (N = 2, 1%). Approximately 54% (N = 94) had no comorbid psychiatric disorder. Table 2 contains information about the use of antipsychotics in dementia patients with comorbid psychiatric conditions. Patients prescribed an antipsychotic and those not prescribed an antipsychotic did not differ significantly in number of diagnoses of mood disorder (41% and 35%, respectively), although patients on antipsychotic treatment were significantly less likely than those not on antipsychotic treatment to have no psychiatric diagnosis ($p < .05$) and significantly more likely to have a thought disorder ($p < .001$). Further, we found that our newly diagnosed, nonaggressive dementia patients prescribed antipsychotics, compared with patients not prescribed antipsychotics (Table 1), were more likely to have delusions (28% vs. 3%, $p < .001$), hallucinations (45% vs. 6%, $p < .001$), and nonaggressive agitation (38% vs. 4%, $p < .001$).

Documentation of Nonpharmacologic Interventions

For the 173 patients, 21 nonpharmacologic interventions were documented for symptoms of dementia. These interventions were documented in only 7% (N = 12) of patients. Caregiver psychoeducation was documented most

frequently (N = 7, 58%). Other nonpharmacologic interventions were as follows: recommendations for changes in patient activity or demands (e.g., changes in routines and scheduling, reduction in amount and complexity of activities) (N = 4, 33%); referral for behavior-specific therapy (N = 4, 33%); referral to social work (e.g., for behavioral problems) (N = 4, 33%); and cognitive intervention (e.g., reorientation, reminders, cues, task sequencing) (N = 2, 17%). In some instances, patients were referred for multiple nonpharmacologic interventions. Less than 50% (N = 5, 42%) of the documented nonpharmacologic interventions occurred before an attempt at a pharmacologic intervention.

Attempts to Decrease or Discontinue Antipsychotic

As mentioned above, 29 patients (17%) were taking antipsychotics. Attempts to either discontinue or decrease the medication were documented for only 2 (7%) of these 29 patients.

DISCUSSION

This study was undertaken to explore 2 research questions. The first was, “What is the prevalence of

antipsychotic use in newly diagnosed, nonaggressive dementia patients?" The second was, "Why are nonaggressive, newly diagnosed dementia patients prescribed antipsychotic medication?" For the first question, we hypothesized that few, if any, newly diagnosed, nonaggressive dementia patients would be prescribed antipsychotics. However, 29 patients (17%) were taking antipsychotics, including 9 nonpsychotic, nonagitated patients (5%). For the second question, we hypothesized that antipsychotics would be prescribed primarily to participants with comorbid psychiatric conditions. However, our study did not show this to be the case.

Given the above findings, we determined that antipsychotic medications are used in a sizable minority of newly diagnosed, nonaggressive dementia patients. Based on our chart-abstraction results, it appears that the prescribing practices of physicians include the prescription of antipsychotic medication to patients exhibiting psychosis and agitation. These findings indicate that patients exhibiting symptoms of psychosis and agitation are at increased risk of antipsychotic prescription. We also found evidence that, once a physician prescribed an antipsychotic for a dementia patient, there were few attempts to modify, taper, or discontinue the medication, as practice guidelines suggest.

This predilection to continue patients on antipsychotic treatment carries over even to acute conditions. Two patients were started on antipsychotic treatment for delirium and remained on it afterwards as outpatients. No practice guidelines suggest long-term use of antipsychotics for delirium.

The use of antipsychotics appears to be less prevalent in nonaggressive patients than in aggressive patients.¹⁹ In our sample, antipsychotic use (17%) is less than that reported in other studies on aggressive dementia outpatients (74%) and less than that reported for dementia outpatients in general (27% to 32%).^{10,20} The rate of antipsychotic use among our sample is also less than the 46% reported in a sample of newly diagnosed, aggressive dementia patients.⁹

We expected that comorbid psychiatric conditions would explain why newly diagnosed, nonaggressive dementia patients are prescribed antipsychotics. However, our data did not support this hypothesis. Practice guidelines also suggest the use of nonpharmacologic interventions for behavioral symptoms before pharmacologic interventions, but our chart-abstraction results found limited use of this practice. Given the rare documentation of nonpharmacologic interventions in general in this population, the many guidelines that advise these interventions,⁵⁻⁸ and the effectiveness of some of these interventions,^{21,22} further work must be done to create clear delivery methods for nonpharmacologic interventions. Specifically, to decrease antipsychotic use and the recently discovered adverse effects of increased cardiovas-

cular accidents, nonpharmacologic interventions should focus on symptoms of psychosis or agitation. Educating physicians about the need for nonpharmacologic interventions, especially in the context of evidence showing lack of effectiveness and an increase in adverse events, must be a goal for future care of dementia patients.

Discontinuation of antipsychotics was rarely documented, despite randomized controlled trials that document the safety and usefulness of such a practice.²³⁻²⁵ Such interventions have been found to be well tolerated and to not result in increased behavioral disturbances. Although current regulations in the nursing home setting require discontinuation trials, there are no such similarly strong policy-level recommendations in the non-nursing home setting.

This study has limitations. First, our records came from only 1 institution; as a result, we cannot examine the extent to which local practice patterns influence our findings. Second, this study was retrospective instead of prospective, although our chart review captured the care provided over an extended period of time. Third, the lack of documentation of a symptom or treatment does not mean that it did not occur; it is possible, for example, that nonpharmacologic interventions were sometimes applied but not documented. Finally, our patient population was specific to veterans and subject to the biases implicit in this population; for example, almost all patients were men.

In summary, a sizable minority of newly diagnosed, nonaggressive dementia patients are taking antipsychotic agents. Prescription practices for these drugs will need to change, and physicians will need greater education and awareness of the benefits of using nonpharmacologic, instead of pharmacologic, interventions.

Drug names: haloperidol (Haldol and others), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal).

REFERENCES

1. Hebert LE, Beckett LA, Scherr PA, et al. Annual incidence of Alzheimer disease in the United States projected to the years 2000 through 2050. *Alzheimer Dis Assoc Disord* 2001;15:169-173
2. Herrmann N, Lanctot KL, Sambrook R, et al. The contribution of neuropsychiatric symptoms to the cost of dementia care. *Int J Geriatr Psychiatry* 2006;21:972-976
3. Murman DL, Colenda CC. The economic impact of neuropsychiatric symptoms in Alzheimer's disease: can drugs ease the burden? *Pharmacoeconomics* 2005;23:227-242
4. Knopman DS, Berg JD, Thomas R, et al, for the members of the Alzheimer's Disease Cooperative Study. Nursing home placement is related to dementia progression: experience from a clinical trial. *Neurology* 1999;52:714-718
5. American Geriatrics Society, American Association for Geriatric Psychiatry. Consensus statement on improving the quality of mental health care in US nursing homes: management of depression and behavioral symptoms associated with dementia. *J Am Geriatr Soc* 2003;51:1287-1298
6. Lyketsos CG, Colenda CC, Beck C, et al. Position statement of the American Association for Geriatric Psychiatry regarding principles of care for patients with dementia resulting from Alzheimer disease. *Am J Geriatr Psychiatry* 2006;14:561-572. Erratum in *Am J Geriatr Psychiatry* 2006;14:808

7. AGS Clinical Practice Committee. Guidelines Abstracted from the American Academy of Neurology's Dementia Guidelines for Early Detection, Diagnosis, and Management of Dementia. *J Am Geriatr Soc* 2003;51:869–873
8. American Psychiatric Association. Practice Guideline for the Treatment of Patients With Alzheimer's Disease and Other Dementias of Late Life. *Am J Psychiatry* 1997;154(suppl 5):1–39
9. Kunik ME, Walgama JP, Snow AL, et al. Documentation, assessment, and treatment of aggression in patients with newly diagnosed dementia. *Alzheimer Dis Assoc Disord* 2007;21:115–121
10. Kolanowski A, Fick D, Waller JL, et al. Outcomes of antipsychotic drug use in community-dwelling elders with dementia. *Arch Psychiatr Nurs* 2006;20:217–225
11. Rochon PA, Stukel TA, Bronskill SE, et al. Variation in nursing home antipsychotic prescribing rates. *Arch Intern Med* 2007;167:676–683
12. Schneider LS, Tariot PN, Dagerman KS, et al. Effectiveness of atypical antipsychotic drugs in patients with Alzheimer's disease. *N Engl J Med* 2006;355:1525–1538
13. Deberdt WG, Dysken MW, Rappaport SA, et al. Comparison of olanzapine and risperidone in the treatment of psychosis and associated behavioral disturbances in patients with dementia. *Am J Geriatr Psychiatry* 2005;13:722–730
14. US Food and Drug Administration. FDA issues public health advisory for antipsychotic drugs used for treatment of behavioral disorders in elderly patients. 2005. Available at <http://www.fda.gov/bbs/topics/ANSWERS/2005/ANS01350.html>. Accessed March 6, 2007
15. Karlawish J. Alzheimer's disease: clinical trials and the logic of clinical purpose. *N Engl J Med* 2006;355:1604–1606
16. Ryden, MB. Aggressive behavior in persons with dementia who live in the community. *Alzheimer Dis Assoc Disord* 1988;2:342–355
17. Cummings JL, Mega M, Gray K, et al. The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. *Neurology* 1994;44:2308–2314
18. Kaufer D, Cummings JL, Ketchel P, et al. Validation of NPI-Q: a brief clinical form of the NPI. *J Neuropsychiatry Clin Neurosci* 2000;12:233–239
19. Alexopoulos GS, Jeste DV, Chung H, et al. The Expert Consensus Guideline Series: Treatment of Dementia and its Behavioral Disturbances. *Postgrad Med* January 2005 (Special Report): 1–111. Available at <http://www.psychguides.com/ecgs16.php>. Accessibility verified Dec 20, 2007
20. Mirakhor A, Craig D, Hart DJ, et al. Behavioural and psychological syndromes in Alzheimer's disease. *Int J Geriatr Psychiatry* 2004;19:1035–1039
21. Livingston G, Johnston K, Katona C, et al. Old Age Task Force of the World Federation of Biological Psychiatry: systematic review of psychological approaches to the management of neuropsychiatric symptoms of dementia. *Am J Psychiatry* 2005;162:1996–2021
22. Ayalon L, Gum AM, Feliciano L, et al. Effectiveness of nonpharmacological interventions for the management of neuropsychiatric symptoms in patients with dementia: a systematic review. *Arch Intern Med* 2006;166:2182–2188
23. Reekum RV, Clarke D, Conn D, et al. A randomized, placebo-controlled trial of the discontinuation of long-term antipsychotics in dementia. *Int Psychogeriatr* 2002;14:197–210
24. Ruths S, Straand J, Nygaard HA, et al. Effect of antipsychotic withdrawal on behavior and sleep/wake activity in nursing home residents with dementia: a randomized, placebo-controlled, double-blinded study: the Bergen District Nursing Home Study. *J Am Geriatr Soc* 2004;52:1737–1743
25. Cohen-Mansfield J, Lipson S, Werner P, et al. Withdrawal of haloperidol, thioridazine, and lorazepam in the nursing home: a controlled, double-blind study. *Arch Intern Med* 1999;159:1733–1740