AMERICAN ACADEMY OF NEUROLOGY

PRACTICE PARAMETER: MANAGEMENT OF DEMENTIA (AN EVIDENCE-BASED REVIEW)

Report of the Quality Standards Subcommittee of the American Academy of Neurology

R.S. Doody, MD, PhD; J.C. Stevens, MD; C. Beck, RN, PhD; R.M. Dubinsky, MD; J.A. Kaye, MD; L. Gwyther, MSW; R.C. Mohs, PhD; L.J. Thal, MD; P.J. Whitehouse, MD, PhD; S.T. DeKosky, MD; and J.L. Cummings, MD

Article abstract—*Objective:* To define and investigate key issues in the management of dementia and to make literature-based treatment recommendations. *Methods:* The authors searched the literature for four clinical questions: 1) Does pharmacotherapy for cognitive symptoms improve outcomes in patients with dementia? 2) Does pharmacotherapy for noncognitive symptoms improve outcomes in patients with dementia? 3) Do educational interventions improve outcomes in patients and/or caregivers? 4) Do other nonpharmacologic interventions improve outcomes in patients and/or caregivers? *Results:* Cholinesterase inhibitors benefit patients with AD (Standard), although the average benefit appears small; vitamin E likely delays the time to clinical worsening (Guideline); selegiline, other antioxidants, anti-inflammatories, and estrogen require further study. Antipsychotics are effective for agitation or psychosis in patients with dementia where environmental manipulation fails (Standard), and antidepressants are effective in depressed patients with dementia (Guideline). Educational programs should be offered to family caregivers to improve caregiver satisfaction and to delay the time to nursing home placement (Guideline). Staff of long-term care facilities should also be educated about AD to minimize the unnecessary use of antipsychotic medications (Guideline). Behavior modification, scheduled toileting, and prompted voiding reduce urinary incontinence (Standard). Functional independence can be increased by graded assistance, skills practice, and positive reinforcement (Guideline).

NEUROLOGY 2001;56:1154-1166

Introduction. *Mission statement.* The Quality Standards Subcommittee (QSS) develops scientifically sound, clinically relevant practice parameters to aid in the practice of neurology. This article addresses pharmacologic and nonpharmacologic treatments for dementia management.

Background and justification. As the US population ages, the incidence and prevalence of various dementias will increase in the absence of new methods for preventing or reversing dementia. The NIH estimates that there will be 8.5 million Americans with Alzheimer's disease by the year 2030, and an unknown number of people with other dementias.[1] This practice parameter is addressed to neurologists and all other clinicians who manage patients with dementia.

Clinical question statement. This practice parameter addresses four clinically relevant questions regarding the management of dementia:

- Does pharmacotherapy for cognitive symptoms improve outcomes in patients with dementia compared with no therapy?

The appointment of authors for this guideline was done in cooperation with the Alzheimer's Association and overlaps significantly with the membership of the Medical and Scientific Advisory Council and the Board of Directors of the association. The Alzheimer's Association agrees with the content of this paper in all important regards.

This guideline has been endorsed by the American Association of Neuroscience Nurses and the American Geriatrics Society.

From the Department of Neurology (Dr. Doody), Baylor College of Medicine, Houston, TX; Lutheran Medical Office (Dr. Stevens), Fort Wayne, IN; Department of Geriatrics (Dr. Beck), College of Medicine, University of Arkansas for Medical Sciences, Little Rock; Department of Neurology (Dr. Dubinsky), University of Kansas Medical Center, Kansas City; Departments of Neurology (Dr. Kaye), Oregon Health Sciences University and Portland Veterans Affairs Medical Center, Portland, OR; Duke University (Ms. Gwyther), Durham, NC; Mount Sinai School of Medicine and VA Medical Center (Dr. Mohs), Bronx, NY; Department of Neurosciences (Dr. Thal), University of California at San Diego; Departments of Neurology (Dr. Whitehouse), Case Western Reserve University and University Hospitals of Cleveland, OH; Departments of Neurology and Psychiatry (Dr. DeKosky), University of Pittsburgh, PA; Departments of Neurology and Psychiatry & Biobehavioral Science (Dr. Cummings), University of California at Los Angeles.

Approved by the AAN Quality Standards Subcommittee November 11, 2000. Approved by the AAN Practice Committee January 6, 2001. Approved by the AAN Board of Directors February 24, 2001.

Received July 10, 2000. Accepted in final form February 9, 2001.

Address correspondence and reprint requests to the Quality Standards Subcommittee, American Academy of Neurology, 1080 Montreal Ave., St. Paul, MN 55116.

- Does pharmacotherapy for noncognitive symptoms improve outcomes in patients with dementia compared with no therapy?
- Do educational interventions improve outcomes in patients and/or caregivers of patients with dementia compared with no such interventions?
- Do nonpharmacologic interventions other than education improve outcomes in patients and/or caregivers of patients with dementia compared with no such interventions?

The work group identified three additional issues that are important and for which clinicians require guidance:

- How does cooperation among neurologists, other clinicians, and community care providers benefit patients?
- How do different economic models of care impact the care of patients with dementia?
- How should physicians evaluate levels of decision-making capacity in their patients with dementia?

This last question is particularly critical, given recently proposed guidelines for research using subjects with impaired capacity to consent.[2] However, the literature searches did not yield sufficient evidence-based articles concerning these special issues to which we could apply the same process used to assess treatment interventions. We mention these special issues in a separate section of this parameter to emphasize the impact of these unanswered questions and the importance of initiating research in these areas.

Process. *Panel selection.* The QSS of the American Academy of Neurology identified two team leaders who in turn identified committee members to participate in the creation of one or more practice parameters on dementia (early detection, diagnosis, and management of dementia). Committee members disclosed any real or potential conflicts of interest.

Literature review process. Search terms. Alzheimer's disease, vascular or multi-infarct dementia, dementia with associated parkinsonian disorder (diffuse Lewy body disease, dementia with Lewy bodies, Parkinson's disease with dementia), progressive supranuclear palsy, frontotemporal dementia (including Pick's disease), and senile dementia. Additional search terms were question-specific:

- Question 1: Cholinesterase inhibitors, antioxidants, hormones, anti-inflammatory agents/drugs, cholinergic agents/drugs, nootropics (class of compounds structurally related to piracetam), metabolic enhancers, neurotrophic agents/drugs, (complementary)alternative medicines, treatment, and pharmacotherapy.
- Question 2: Hypnotics, antidepressants, anxiolytics, tranquilizers, sleep medications, selective serotonin reuptake inhibitors (SSRI), treatment and sleep, treatment and depression, treatment and anxiety, treatment and agitation, treatment and disinhibition, treatment and affective disorders, management, treatment and maintain (trunc), and treatment and discontinue (trunc).
- Questions 3 and 4: Counseling, education and caregiver, education and patient, environment, behavior (trunc) manag (trunc), behavior (trunc) and modif (trunc), advance directive, rehabilitation, and terminal care.

The key and index words for the special issue of cooperation between specialists were the following: treatment and multidisciplinary, treatment and team, treatment and community, neurologist (trunc), primary care, respite care, services, providers, transfer of care, long-term care, and family advocacy. Special issues related to economic models used the following key and index words: health care systems, health maintenance organization, preferred provider organization, medicaid, medicare, insurance, managed care, economic (trunc), and quality of care. Special issues related to determining capacity to consent used were the following: competency, decision making, patient refusal of therapy/treatment, physician patient relations, patient rights, patient involvement, and informed consent.

Databases. For questions 1 and 2 the following databases were searched: MEDLINE, Embase, Current Contents, Psych Abstracts, and Cochrane databases. For questions 3 and 4: MEDLINE, Embase, Current Contents, Psychology Info, Cochrane, and CINAHL.

Inclusion/exclusion criteria and process. Studies selected included the following: randomized, controlled studies in all languages and other types of studies limited to English; human subjects with N greater than 20, regardless of outcome measured; and review articles published between January 1998 and November 1999. The nonpharmacologic intervention questions allowed smaller N for supporting studies to reflect the activity in the field. Members of the work group reviewed all search results and the bibliographies of the review articles to identify any articles that they thought were missing; these articles were submitted to the same inclusion/exclusion criteria. The initial search was conducted in October 1998; additional articles were added until July 2000.

Table 1 *Classification of evidence*

Class	Description
I	Evidence provided by one or more well designed, randomized, controlled clinical trials, including overviews (meta-analyses) of such trials.
II	Evidence provided by well designed observational studies with concurrent controls (e.g., case control or cohort studies).
III	Evidence provided by expert opinion, case series, case reports, and studies with historical controls.

Table 2 *Levels of recommendations*

Recommendation	Level of evidence
Standard	Principle for patient management that reflects a high degree of clinical certainty (usually this requires Class I evidence that directly addresses the clinical questions, or overwhelming Class II evidence when circumstances preclude randomized clinical trials).
Guideline	Recommendation for patient management that reflects moderate clinical certainty (usually this requires Class II evidence or a strong consensus of Class III evidence).
Practice Option	Strategy for patient management for which the clinical utility is uncertain (inconclusive or conflicting evidence or opinion).

Number and disposition of articles, data extraction, and classification of evidence. The search strategy identified 2,548 articles. A total of 380 met the predefined inclusion/exclusion criteria and were reviewed by at least two individuals. Selected items from each article were entered into a standardized data extraction form, and each article was assigned a class of evidence based upon a priori definitions (table 1), which determined whether or not study results were ultimately translated into Standards, Guidelines, or Practice Options (table 2).

Development of evidence tables. For all extracted articles, evidence tables were developed according to search question. These tables indicate the author and year of the study, level of evidence, main purpose of the study, population, intervention, outcome measures, and results.

Internal and external review of the document. The first author drafted the document with input and approval from other work group members. After QSS review and approval, the document was circulated to the members of the full Dementia Practice Parameter work group (committee members drafting the early detection and diagnosis of dementia sections), members of the AAN Member Review Network, appropriate sections of the AAN, US and international dementia experts, and selected patient advocacy and physician organizations.

Analysis of evidence. *Does pharmacotherapy for cognitive symptoms improve outcomes in patients with dementia compared with no therapy?*

Alzheimer's disease. Cholinesterase inhibitors. Tacrine has been tested for efficacy in the management of dementia in six studies involving more than 2,000 subjects. Approximately 25% of patients treated with the highest dose (160 mg/day) were stabilized and exhibited less decline on global cognitive testing and on a clinician's global evaluation compared with placebo-treated patients.[3,4] Only approximately 25% of patients assigned high doses completed the studies because of adverse events (including elevated transaminase levels in approximately 50% of subjects). Tacrine requires four times daily administration (10 mg QID for 4 weeks, then 20 mg QID for 4 weeks, then 30 mg QID for 4 weeks, then 40 mg QID with dosage escalation as tolerated) with hepatotoxicity monitoring every other week from weeks 4 to 16, then every 3 months. [3-9]

In three double-blind, placebo-controlled trials enrolling more than 1,000 subjects, donepezil produced a significant drug–placebo difference in trials lasting for 12 to 24 weeks on both a composite neuropsychologic test and a clinician's global evaluation.[10-13] Efficacy has been demonstrated at doses of 5 and 10 mg. Side effects occurred in up to 17% of subjects exposed to the drug, and there were not reports of hepatotoxicity. The dose is 5 mg QD (can be given at bedtime, but this is not necessary) and can be increased to 10 mg QD after 4 to 6 weeks.

Treatment with rivastigmine tartrate for 26 weeks resulted in significant differences compared with placebo in cognition and on a clinician's global assessment and an activities of daily living scale.[14-16] Subjects on higher doses (6 to 12 mg per day) performed better than those on lower doses (1 to 4 mg per day, not different from placebo in one study). Side effects (including weight loss) were present in up to 50% of individuals in higher-dose groups and led to discontinuation of the drug in up to 25%.[14-16] The initial dose is 1.5 mg BID, which can be increased to 3 mg BID, then 4.5 mg BID, then 6 mg BID with a minimum of 2 weeks between increases.

Galantamine was tested in more than 1,600 subjects with mild to moderate AD in two double-blind, placebo-controlled studies. Treatment with galantamine (16 to 32 mg per day) resulted in significant cognitive improvement on the Alzheimer's Disease Assessment Scale–Cognitive Subscale (ADAS–Cog), the clinician's global assessment, the activities of daily living scale, and a behavior scale. Efficacy was present at 16 mg/day and 24 mg/day. Side effects occurred in up to 13% at 16 mg per day and up to 17% of subjects exposed to 24 mg per day.[17,18] The drug has been approved by the FDA (16 and 24 mg/day).

Development of controlled-release physostigmine,[19,20] metrifonate,[21-23] velnacrine,[24,25] and eptastigmine[26-28] were discontinued because of unacceptable toxicities.

Conclusions. Significant treatment effects have been demonstrated with several different cholinesterase inhibitors, indicating that the class of agents is consistently better than placebo. However, the disease eventually continues to progress despite treatment, and the average "effect size" is modest (Appendix B). Global changes in cognition, behavior, and functioning have been detected by both physicians and caregivers, indicating that even small measurable differences may be clinically significant. To date, there have been no head-to-head comparisons of cholinesterase inhibitors, and the main differences between these agents are in the side-effect profiles and the ease of administration (e.g., once or twice versus four times daily dosing).

Precursors and agonists to improve cholinergic neurotransmission in AD. Results of two precursor therapy trials using lecithin[29-30] and one study of a relatively selective M1 agonist (Lu25-109)[31] were negative for treatment of AD. Other muscarinic agonists, including xanomeline[32] and SB202026,[33] produced small drug–placebo differences on the ADAS-Cog but not on a global measure, which should be present to support the clinical significance of such statistical differences. Muscarinic agonists were associated with significant side effects that likely limited the maximum tolerated dose needed to improve cognition.

Conclusions. Current studies do not support the efficacy of cholinergic precursors or muscarinic agonists for the treatment of AD. It is unclear whether highly selective M1 agonists, delivered in adequate doses to the CNS, would be beneficial and tolerable in AD.

Table 3 *Drugs reviewed in this article*

Cognitive		
Acetyl-L-carnitine	Gingko biloba	Pentoxifylline
ACTH4-9 analog	Glycosamine	Phosphatidyl serine
Alpha-tocopherol (Vitamin E)	Hydergine	Physostigmine-CR
Aniracetam	Ibuprofen	Piracetam
Besipiridine	Idebenone	Prednisone
BMY21, 501	Indomethacin	Premarin (estrogen)
Cerebrolysin	Lecithin	Propentofylline
Cyclandelate	Lu25-109	Pyritonol
Cycloserine	Memantine	Rivastigmine
DGAVP	Metrifonate	SB202026
Diclofenac	Milacemide	Selegiline
Donepezil	Naftidrofuryl	Tacrine
Eptastigmine	Nicergoline	Velnacrine
Flunarizine	Nicotine	Vincamine
Fluvoxamine	Nimodipine	Xanomeline
Galantamine	Oxiracetam	Xantinolnicotinate
Noncognitive		
Amitryptyline	Haloperidol	Oxazepam
Carbamazepine	Imipramine	Paroxetine
Citalopram	L-deprenyl	Quetiapine
Clomipramine	Maprotiline	Risperidone
Desferroxamine	Meprerone	Tiapride
Diphenhydramine	Metrifonate	Thioridazine
Fluoxetine	Moclobemide	Xanomeline
Fluvoxamine	Nicergoline	
Galantamine	Olanzepine	

Other cognitive-enhancing agents in AD. In a single trial, nicotine produced improvement on several neuropsychologic measures in patients with AD but produced increased anxiety.[34] Intravenous cerebrolysin, a neurotrophic brain extract, improved global functioning and activities of daily living in one trial.[35] Several negative studies have been reported for treatment in AD including an ACTH4-9 analog,[36] DGAVP;[37] the nootropics aniracetam,[38] BMY21, 501[39] and piracetam;[40] and two trials of phosphatidyl serine.[41,42] Other negative Class I studies include the NMDA receptor stimulator cycloserine,[43] besipiridine,[44] and milacemide.[45] Hydergine (Novartis, East Hanover, NJ) was ineffective at 3 mg per day[46] and showed slight memory improvement at 6 mg day, but did not meet a priori benefit standards.[47] Patients receiving acetyl-L-carnitine, a membrane-stabilizing agent, showed less decline over one year on 4 of 14 neuropsychologic measures,[48] but the drug was ineffective in a second study.[49] Idebenone, a coenzyme Q analog, showed mild improvement in some neuropsychologic tests[50] and produced a significant drug–placebo difference on a global neuropsychologic instrument,[51] but in separate studies. Selegiline produced a modest drug–placebo difference in cognition in a 3-month trial of 136 patients with mild to moderate AD[52] but not in a 6-month trial with 60 patients.[53] A low dose (30 mg TID) of nimodipine improved memory (but not other measures) but not at a higher dose (90 mg TID).[54]

Conclusions. A wide group of agents with diverse mechanisms of action have been tested in at least one Class I trial, but there is incomplete or conflicting evidence for these agents.

Other strategies to slow decline in AD. In one large, 2-year trial, selegiline (5 mg BID) and vitamin E (1,000 I.U. [alpha-tocopherol] BID) significantly delayed the time to a composite outcome of primary measures indicative of clinical worsening, and fewer patients treated with vitamin E were institutionalized.[55] Importantly, there was no additive effect from selegiline plus vitamin E, neither agent improved cognitive function (ADAS–Cog) compared with baseline values, and those on drug did not decline less than those on placebo on these types of measures.

Although epidemiologic data suggest that anti-inflammatory drugs may be protective against the development of AD,[56] few anti-inflammatory drug trials have been reported. In one 6-month trial of indomethacin, stabilization of cognition was suggested, although the authors reported a 44% dropout rate.[57] A 6-month trial of diclofenac for treatment of AD reported slightly slower decline (not significant) and a 50% dropout rate because of adverse events.[58] A recent trial of prednisone for the treatment of AD was negative.[59] Epidemiologic studies suggest that estrogen may be protective against the development of AD, and from this observation, the possibility that it also might have a therapeutic effect in AD has been suggested. To date, two well designed clinical trials examining the ability of Premarin® (Wyeth–Ayerst, Philadelphia, PA) to slow the rate of decline in women with AD were negative.[60,61]

Conclusions. One study suggests a possible benefit of vitamin E or possibly selegiline for treatment of AD. The agents should not be combined. The use of anti-inflammatory agents, prednisone, and estrogen to prevent the progression of AD are not supported by prospective data.

Drugs tested in mixed dementia populations or in patients with mixed dementias. In one trial, propentofylline (a glial-modulating agent) produced a drug–placebo difference on a variety of cognitive and global measures,[62] but these findings were not adequately replicated in a second trial. Memantine, an NMDA receptor antagonist, improved cognition and global functioning in two poorly defined groups of patients with dementia.[63-65] Several nootropic agents including oxiracetam,[66-68] nicergoline,[69,70] vincamine,[71] naftidrofuryl,[72] and xantinolnicotinate[73] have shown small degrees of improvement on some outcomes for mixed dementia populations. None of these agents has been adequately tested for specific types of dementia. One trial reported a mild benefit of fluvoxamine.[74] Treatment with various formulations of gingko biloba was associated with significant improvements in some (but not all) a priori parameters including a small treatment–placebo difference on a cognitive measure (not detected on a clinical global),[75] some improvement on a clinician's global assessment and an activities of daily living scale,[76] and increased speed on a subset of timed tasks.[77] Several other agents including glycosamine[78] nimodipine,[79] pyritonol,[80] and acetyl-L-carnitine[81] all have shown small improvements in overall functioning in populations with patients with mixed dementia, but none proved a treatment benefit on all the primary outcome measures.

Conclusions. Ginkgo biloba was safe in one Class I trial of patients with mixed dementia, but benefits fall short of those expected for clinically effective antidementia treatments (e.g., a psychometric measure and a clinician's global). Currently there are no adequately controlled positive trials supporting the use of any pharmacologic agents in patients believed to have mixed neurodegenerative and ischemic vascular dementia, or in populations in which the specific type of dementia is not identified.

Ischemic vascular (multi-infarct) dementia. Few Class I trials have been performed in populations with pure ischemic vascular or multi-infarct dementia. In a single study of the nootropic oxiracetam,[82] improved functioning on the Blessed Functional scale was reported. Cyclandelate and flunarizine showed pre- to posttreatment benefits on a subset of measures.[83] Two trials of pentoxifylline were negative.[84,85]

Practice recommendations.

Pharmacologic treatment of AD.

- Cholinesterase inhibitors should be considered in patients with mild to moderate AD (Standard), although studies suggest a small average degree of benefit.
- Vitamin E (1000 I.U. PO BID) should be considered in an attempt to slow progression of AD (Guideline).
- Selegiline (5 mg PO BID) is supported by one study, but has a less favorable risk–benefit ratio (Practice Option).
- There is insufficient evidence to support the use of other antioxidants, anti-inflammatories, or other putative disease-modifying agents specifically to treat AD because of the risk of significant side effects in the absence of demonstrated benefits (Practice Option).
- Estrogen should not be prescribed to treat AD (Standard).

Mixed populations or patients with mixed dementias.

- Some patients with unspecified dementia may benefit from ginkgo biloba, but evidence-based efficacy data are lacking (Practice Option).

Ischemic vascular dementia.

- There are no adequately controlled trials demonstrating pharmacologic efficacy for any agent in ischemic vascular (multi-infarct) dementia.

Recommendations for future research. Cholinesterase inhibitors are the mainstay of treatment for patients with mild to moderate AD. Insufficient data exist on the effectiveness of cholinesterase inhibitors in patients with mild cognitive impairment (MCI), early AD, and severe AD, although studies are underway to examine these issues. Antioxidants and anti-inflammatories are under study for the ability to delay the progression of MCI to AD. Comparative trials assessing multiple cholinesterase inhibitors and add-on studies combining cholinesterase inhibition with other therapeutic strategies are needed.

Additional well designed, adequately powered studies using common outcome measures would be beneficial regarding the efficacy of ginkgo biloba, cerebrolysin, piracetam, Hydergine, acetyl-L-carnitine, nimodipine, ibuprofen, and other anti-inflammatory agents. Additional studies comparing different formulations and doses of vitamin E and other antioxidant agents are needed to assess the impact of these agents in altering disease progression of AD.

Ischemic vascular dementia requires clear diagnostic criteria, recognition and definition of subgroups of patients, and an understanding of the natural history of various forms of this disorder. Clinical trials must use standard diagnostic

criteria and may require subgrouping of patients into populations with large vessel disease versus small vessel disease. Such advances in diagnostic specificity may provide a way to test efficacy of proposed therapeutic agents and treatment strategies. Other non-AD dementias, such as dementia with Lewy bodies (DLB) and frontotemporal dementia, lack definitive Class I treatment studies, but very recent data suggesting that cholinesterase inhibitors benefit patients with DLB should be confirmed.

Does pharmacotherapy for noncognitive symptoms improve outcomes for patients with dementia and/or their caregivers compared with no therapy? *Treatment of behavioral disturbances.* It is well accepted that agitation may be due to identifiable causes (such as pain) or associated with environmental triggers that can be avoided. If evaluation for these conditions does not suggest a nonpharmacologic strategy, medications should be considered. One study showed that risperidone was beneficial compared with placebo for the treatment of psychosis and aggression.[86] A single study compared risperidone versus haloperidol or placebo and reported efficacy for risperidone over placebo, with fewer side effects than haloperidol.[87] One study also supports the efficacy of olanzepine over placebo for reducing agitation and psychosis as measured by the Neuropsychiatric Inventory.[88] High doses of haloperidol (2 to 3 mg/day) were shown to be more effective than low doses (0.5 to 0.75 mg QD) or placebo.[89] One study demonstrated some differences favoring risperidone over haloperidol and thioridazine.[90] Another study compared haloperidol to oxazepam and diphenhydramine for agitation and psychosis and showed little difference in their efficacy.[91] However, there are no studies that compare atypical antipsychotic agents (e.g., risperidone, olanzepine, and quetiapine) to antihistiminics or benzodiazepines. One study showed global improvement of agitation in patients with dementia treated with the antipsychotic agents tiapride and meperone, but there was no placebo control.[92]

Most of these studies focused on mixed populations of patients with dementia, so it is not possible to assess a medication's relative efficacy in specific forms of dementia. One observational study suggests that patients who have DLB may be more sensitive to neuroleptics, and several deaths have been reported within weeks of starting such agents in these patients, although the study was not designed to determine causality.[93]

Only one randomized study that meets our criteria has been published to date on the use of L-deprenyl to treat agitation, psychosis, and depression in dementia, and this study failed to show consistent benefits.[53] The beneficial effect on behavior of cholinesterase inhibitors (galantamine, metrifonate)[17,18,22] and a muscarinic cholinergic agonist (xanomeline)[32] includes a delay or decrease in the emergence of behavioral disturbances, as well as a reduction in existing problem behaviors. One study also suggests that nicergoline may benefit behavioral disturbances.[94]

The chelating agent, desferroxamine, was reported to benefit behavior on a nonstandardized video-rating scale.[95] Carbamazepine was studied in the treatment of agitation and psychosis and reported benefits.[96] The antidepressant agent citalopram was proposed as a treatment for agitation in a poorly defined population with "cognitive deficits."[97]

Depression. One study showed no difference between imipramine and placebo for treatment of depression in patients with AD, largely because of improvement in both the treated and untreated groups.[98] Two small studies suggested benefits for clomipramine[99] and moclobemide.[100] Another study suggested that maprotiline may have beneficial effects on depression, but the study results are compromised by a high rate lost to follow-up.[101]

A few small studies suggested that the use of serotonergic reuptake blockers such as fluvoxamine,[74] fluoxetine,[102] citalopram,[97] and paroxetine[103] may offer some benefit in treating depression in patients with AD. One study compared fluoxetine to amitriptyline and showed improved depression scores for both groups, but there were more dropouts because of side effects in the amitriptyline group.[102]

Conclusions. Class I evidence supports the use of both traditional and atypical antipsychotics in the treatment of agitation and psychosis in dementia, and atypical agents seem to be better tolerated. There is little evidence to support the use of other agents such as anticonvulsants, benzodiazepines, antihistaminics, monoamine oxidase inhibitors, or SSRI for the treatment of agitation or psychosis in dementia. For treatment of depression, SSRI may offer some benefit with better tolerability than other antidepressants.

Practice recommendations.

- Antipsychotics should be used to treat agitation or psychosis in patients with dementia where environmental manipulation fails (Standard). Atypical agents may be better tolerated compared with traditional agents (Guideline).
- Selected tricyclics, MAO-B inhibitors, and SSRI should be considered in the treatment of depression in individuals with dementia with side effect profiles guiding the choice of agent (Guideline).

Recommendations for future research. To date, there is no published Class I evidence on pharmacologic treatment for anxiety, disinhibition, sleep disturbance, wandering, shadowing, compulsive behaviors, and apathy.

Additional studies are needed to determine which behavioral symptoms are best treated by nonpharmacologic interventions, with or without the use of concomitant medications. Studies are needed comparing anxiolytics, tricyclic antidepressants, and SSRI for the treatment of depression and anxiety and comparing typical and novel antipsychotics.

Do educational interventions (Appendix C) improve outcomes for patients with dementia and/or their caregivers compared with no interventions? Studies comparing the impact of short-term educational programs to no treatment[104,105] or to participation in support group programs[106,107] found that although participants usually like the educational programs, their impact on patients and caregivers is modest and there is no effect on disease severity or patient outcome. Short-term improvement in caregivers' disease knowledge[104] and ability to cope[104,107] occurs in some studies, although decision-making skills and perceived caregiver burden are not necessarily improved. A computer-based decision support help system improved caregiver confidence but had no effect on patient outcome or caregiver knowledge.[108]

An intensive long-term education and support program for caregivers delayed time to nursing home placement by 12 to 24 months.[109] Additionally, caregiver education improved caregiver health ratings but had no effect on disease symptoms or problem behaviors.[109] A second study included counseling as an intervention but also provided services (support group therapy) to caregivers and found that these interventions delayed the time to nursing home placement by about a year.[110]

One study demonstrated that specialized training of staff in nursing homes can significantly reduce the use of antipsychotic medications in patients with AD, and this study also reported no increase in problem behaviors.[111]

Conclusions. Evidence from Class II and III studies suggests that short-term educational programs are well liked by family caregivers and can lead to a modest increase in disease knowledge and greater confidence among caregivers. Extensive training for caregivers may lead to delayed nursing home placement. Educational training for staff of long-term care facilities can decrease the use of antipsychotic medications without increasing the rate of disruptive behaviors.

Practice recommendations.

- Short-term programs directed toward educating family caregivers about AD should be offered to improve caregiver satisfaction (Guideline).
- Intensive long-term education and support services (when available) should be offered to caregivers of patients with AD to delay time to nursing home placement (Guideline).
- Staff of long-term care facilities should receive education about AD to reduce the use of unnecessary antipsychotics (Guideline).

Recommendations for future research. Intensive, long-term educational programs are not generally available, but research should continue to determine whether they are an effective way to delay nursing home placement in some patients with dementia. Multifaceted programs should either be easily replicated or should be studied in such a way as to identify which components are the most important for achieving the desired outcomes. Future studies must assess long-term outcome, such as quality-of-life measures, to determine the impact of educational interventions on patients and their caregivers.

Do nonpharmacologic interventions other than education improve outcomes for patients and their caregivers compared with no such interventions? *Interventions to improve functional performance.* Graded assistance (Appendix D) supplemented by practice and positive reinforcement was shown to improve performance in daily activities in patients with dementia.[112-117] Behavior modification, scheduled toileting, and prompted voiding reduced urinary incontinence.[118,119] Reactivating occupational rehabilitation (memory training, manual/creative activities, improving sensorimotor functions, and self-management therapy) proved more efficient in improving cognitive performance, psychosocial functioning, emotional balance, and subjective well-being than functional rehabilitation (functional occupational therapy, physiotherapy, and speech therapy).[120] Environment modifications such as low light and nature sounds increased eating behaviors in a preliminary report.[121] Multistrategy group therapies including reality orientation, remotivation, sensory stimulation and integration, reminiscence, and exercises improved activities of daily living.[122,123]

Conclusions. Two Class I studies show that behavior modification, scheduled toileting, and prompted voiding can reduce urinary incontinence. One Class I study, supported by Class II and Class III data, shows that graded assistance, skills practice, and positive reinforcement can increase functional independence in persons with dementia.

Nonpharmacologic interventions for problem behaviors. Music (of the patient's preference)[124] reduced agitation, aggression, and mood disturbance under various conditions including eating and bathing.[125-132] One-on-one social interaction or videotapes of family members reduced verbally disruptive behaviors more than music.[127] However, there are conflicting preliminary reports of the benefits of using familiar audiotaped voices (simulated presence therapy) in improving mood, aggression, and agitation.[133,134] Bright light appeared to reduce aggression, agitation, and diverse behavioral disturbances in small samples of persons with dementia.[135-137] Written cues for repetitive questions/statements from persons with dementia helped diminish those vocalizations in a small study.[138] Walking and light exercise appeared to reduce wandering, aggression, and agitation on preliminary findings;[139,140] however, there are conflicting reports for the benefits of massage therapy in reducing similar behaviors.[141-143]

Many psychosocial interventions have been reported to reduce problem behaviors in patients with dementia including: 1) rigorous psychosocial therapy activities (music, exercise, crafts, and relaxation) combined with staff training;[144] and 2) individualized care and environmental alterations using Piagetian levels of cognitive development,[145] client-oriented care approach,[146] and structured sessions of meditation, relaxation, sensory awareness, and guided imagery (small pilot study).[147] Pet therapy was reported to improve socialization,[148] and a psychomotor activation program had significant beneficial effect on cognition but tended to increase rebellious and negative behavior.[149] Cognitive remediation intervention and social interaction using observational learning and participant modeling reduced disruptive behavior for persons with mild to moderate dementia living in the community.[150] Commands given above the patient's comprehension level increased agitated behaviors in a small study.[151] Several psychosocial interventions, including sensory intervention[152] and other specific individual care plans,[153] have proven ineffective for treatment of problem behaviors.

Alzheimer's special care units. Numerous Class II and Class III studies suggest that special care units (SCU) reduced patient agitation, use of restraints, and catastrophic reactions.[154,155] Specialized staff training within these SCU resulted in reduced behavioral disturbances and decreased use of psychotropic drugs and physical restraints.[156] Similarly, inpatient stays, sometimes coupled with outpatient programs for patients with dementia, were effective in reducing agitation.[157] Patients in a dementia SCU that used a palliative care philosophy showed lower levels of observed discomfort, fewer transfers to acute medical settings, and lower medical costs.[158] Use of exterior space (patient-safe) decreased patient violence and injury reports in nursing homes compared with those that had no exterior spaces[159]; however, remodeling of exterior spaces or interior spaces to resemble nature and home scenes had no apparent benefits in reducing problematic behaviors.[159-162] Transferring patients from long-term care institutions to small, group-living, homelike physical settings with individualized psychosocial and integrity-promoting therapy decreased agitation and restlessness in persons with AD.[163]

Conclusions. Sensory stimulation of various types (auditory, visual, tactile) are usually included as part of a complex, multifaceted approach, so it is difficult to make conclusions about its efficacy. Psychosocial interventions directed towards patients may benefit them, but the a priori outcome measures are often negative and the programs are not easily replicated. The therapeutic benefits of special environments are difficult to evaluate but may have a beneficial impact on agitation.

Psychosocial interventions for caregivers. Data from four Class I studies support the benefits of caregiver interventions that go beyond education to include various forms of support or management techniques: 1) an interdisciplinary psychoeducational family group intervention;[164] 2) extensive individual and family counseling with support groups;[110,165] and 3) home management training for behavioral problems using Progressively Lowered Stress Threshold model.[166] These interventions delayed nursing home placement and reduced caregiver depression, tension, anger, fatigue, and confusion. In contrast, other support-based programs have had minimal effects on caregiver morbidity and burden,[167] caregiver depression and anxiety, and time to patient nursing home placement compared with conventional community nursing.[168]

Caregivers who used respite services (institutional, day center, or in-home services) maintained their relatives with dementia in the community (average of 22 days) longer than caregivers who did not use the services. However, there are conflicting results on caregiver satisfaction, burden, and mental health compared with those who do not use respite services.[169,170] Caregivers who used adult day care and other services had lower levels of caregiving-related stress and better psychological well being.[171] Caregivers using a medical-type of adult day care had significantly more paid help and caregiver burden than did caregivers of patients with dementia using a social subtype of adult daycare.[172] Group counseling increased morale, knowledge, and activities during visits for relatives of patients with dementia in a Class III study.[173] Use of computer network information, telephone support programs, and telephone mini-lecture series have yielded conflicting results on caregiver outcomes.[108,174]

Conclusions. Psychosocial interventions directed toward caregivers, including education, support, and respite care, may improve caregivers' emotional well being and quality of life and may delay nursing home placement for patients with dementia.

Practice recommendations.

Functional performance.

- Behavior modification, scheduled toileting, and prompted voiding should be used to reduce urinary incontinence (Standard).
- Graded assistance, practice, and positive reinforcement should be used to increase functional independence (Guideline).
- Low lighting levels, music, and simulated nature sounds may improve eating behaviors for persons with dementia, and intensive multimodality group training may improve activities of daily living, but these approaches lack conclusive supporting data (Practice Options).

Problem behaviors.

- Persons with dementia may experience decreased problem behaviors with the following interventions: music, particularly during meals and bathing (Guideline); walking or other forms of light exercise (Guideline).
- Although evidence is suggestive only, some patients may benefit from the following (Practice Options):
  - Simulated presence therapy, such as the use of videotaped or audiotaped family
  - Massage
  - Comprehensive psychosocial care programs
  - Pet therapy
  - Commands issued at the patient's comprehension level
  - Bright light, white noise
  - Cognitive remediation

Care environment alterations.

- Although definitive data are lacking, the following environments may be considered for patients with dementia (Practice Options):
  - Special care units (SCU) within long-term care facilities
  - Homelike physical setting with small groups of patients as opposed to traditional nursing homes
  - Short-term, planned hospitalization of 1 to 3 weeks with or without blended inpatient and outpatient care
  - Provision of exterior space, remodeling corridors to simulate natural or home settings, and changes in the bathing environment

Interventions for caregivers.

- The following interventions may benefit caregivers of persons with dementia and may delay long-term placement (Guidelines):
  - Comprehensive, psychoeducational caregiver training
  - Support groups
- Additional patient and caregiver benefits may be obtained by use of computer networks to provide education and support to caregivers (Practice Option), telephone support programs (Practice Option), and adult day care for patients and other respite services (Practice Option).

Recommendations for future research. Studies are needed to identify which patients with dementia are most likely to improve their functional performance through behavioral interventions. Studies should evaluate the efficacy of auditory, exercise, touch, visual, and psychosocial interventions, alone and in combination with pharmacotherapy, for specific problem behaviors. A better understanding is needed on how to calculate the staffing patterns needed to provide appropriate behavioral interventions in long-term care settings. Based on preliminary data, more study on the benefits of small group living versus ward-style, institutional living is warranted. In the area of caregiver support, research is needed to develop ways to match caregiver interventions to the specific needs of caregivers, and to identify the support group processes that contribute to both positive and negative outcomes. Finally, researchers should conduct cost-effectiveness studies of behavioral interventions, care environment alterations, and caregiver interventions.

Special issues regarding the management of patients with dementia. First, more research is needed to define the roles of various types of practitioners (e.g., neurologists, psychiatrists, geriatricians, primary care physicians) in the care of patients with dementia. The benefits of an interactive care approach involving multiple practitioners, including cost–benefit assessments, must be studied. Research leading to guidelines for the cooperation between clinicians is needed because AD is a chronic illness requiring coordinated and changing management over its course.

Second, studies should explore the impact of different models of health care delivery (e.g., HMO, Standard Medicare, and other fee-for-service) specifically on persons with dementia. These health economic studies must consider the differential approach of different payers to coverage for prescription drugs in their models. Such studies should also examine the shifts in health care costs that occur over the course of the disease (e.g., family costs, third-party payer costs, government costs) and should seek equitable solutions that benefit patients and families but do not overburden one portion of the health care sector (e.g., Medicaid).

Finally, more evidence-based studies must explore the benefits of various assessments for predicting capacity to consent for patients with dementia.[174,175] These should include prospective studies of elderly at-risk individuals prior to the development of dementia, as well as studies designed to guide routine clinical care and research involving patients with dementia. Guidance in these areas is critical for therapeutic research to continue effectively in this country.

Disclaimer. This statement is provided as an educational service of the American Academy of Neurology. It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use specific procedures. Neither is it

intended to exclude any reasonable alternative methodologies. The AAN recognizes that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on all the circumstances involved.

Acknowledgment
The authors thank Wendy Edlund, Alison Nakashima, and James Stevens, MD, of the AAN for their enthusiasm for the project and guidance through the evidence-based approach; Ms. Vicki Glasgow of the University of Minnesota Biomedical Library for her assistance in the literature searches; and Starr Pearlman, PhD, for her assistance in editing and compiling the final versions of this document.

Appendix A
Quality Standards Subcommittee Members: Gary Franklin, MD, MPH, Co-Chair; Catherine Zahn, MD, Co-Chair; Milton Alter, MD, PhD; Stephen Ashwal, MD; John Calverley, MD; Richard M. Dubinsky, MD; Jacqueline French, MD; Micheal Glantz, MD; Gary Gronseth, MD; Deborah Hirtz, MD; Robert G. Miller, MD; James Stevens, MD, Facilitator; and William Weiner, MD.

Appendix B
There is no standard approach to determining the effect size of antidementia agents. The effects can be quantified by examining percentages of responders, although any definition of response is arbitrary as is the time point selected to look for response. Patients who respond early can be missed if the time point for assessing response occurs at the end of the study, even if they progress more slowly because of treatment. Effect can be estimated by comparing drug-treated group means to placebo means, and by this estimate cholinesterase inhibitor benefits range from 2 to 5 points on the ADAS–Cog, a 70-point measure of cognitive functioning. The treatment–placebo differences are largely secondary to continuing decline on the part of the placebo patients and temporary stabilization of the treated cohort during 3 to 6 month studies. Effect can also be estimated by comparing the cumulative group responses for treated and placebo patients. By this method, the cholinesterase inhibitors appear to benefit all patients (the response curves are shifted compared with placebo) but to variable degrees.

Appendix C
For purposes of this guideline, the term "educational intervention" refers to structured interactions between a caregiver and an expert on the care of patients with AD designed primarily to enhance the caregiver's knowledge about AD and its management.

Appendix D
Graded assistance is a spectrum of assistance from verbal prompts to physical demonstration, physical guidance, partial physical assistance, and complete physical assistance aimed to provide the least amount of help possible.

References
1. National Institutes of Health, National Institute on Aging. Progress report on Alzheimer's disease, 1999 (NIH Pub. No. 99-4664). Bethesda, MD: US Department of Health and Human Services, 1999.
2. US National Bioethics Advisory Commission. Research involving persons with mental disorders that may affect decisionmaking capacity. Rockville, MD: National Bioethics Advisory Commission, 1998.
3. Farlow M, Gracon S, Hershey L, et al. for the Tacrine Study Group. A controlled trial of Tacrine in Alzheimer's disease. JAMA 1992; 268: 2523–2529.
4. Knapp M, Knopman D, Solomon P, et al. for the Tacrine Study Group. A 30-week randomized controlled trial of high-dose Tacrine in patients with Alzheimer's disease. JAMA 1994; 271: 985–991.
5. Watkins P, Zimmerman H, Knapp M, et al. Hepatotoxic effects of Tacrine administration in patients with Alzheimer's disease. JAMA 1994; 271: 992–998.
6. Chatellier G, Lacombiez L on behalf of Groupe Francais d'Etude de la Tetrahydroaminoacridine. Tacrine (tetrahydroaminoacridine; THA) and lecithin in senile dementia of the Alzheimer type: a multicentre trial. Br Med J 1990; 300: 495–499.
7. Davis K, Thal L, Gamzu E, et al. A double-blind, placebo-controlled multicenter study of Tacrine for Alzheimer's disease. N Engl J Med 1992; 327: 1253–1259.
8. Eagger S, Levy R, Sahakian B. Tacrine in Alzheimer's disease. Lancet 1991; 337: 989–992.
9. Gauthier S, Bouchard R, Lamontagne A, et al. Tetrahydroaminoacridine-lecithin combination treatment in patients with intermediate-stage Alzheimer's disease: results of a Canadian double-blind, crossover, multicenter study. N Engl J Med 1990; 322: 1272–1276.
10. Rogers S, Doody R, Mohs R, et al. and the Donepezil Study Group. Donepezil improved cognition and global function in Alzheimer's disease. Arch Intern Med 1998; 158: 1021–1031.
11. Rogers S, Farlow M, Doody R, et al. and the Donepezil Study Group. A 24-week, double-blind, placebo-controlled trial of donepezil in patients with Alzheimer's disease. Neurology 1998; 50: 136–145.
12. Burns A, Rossor M, Hecker J, et al. and the International Donepezil Study Group. The effects of donepezil in Alzheimer's disease: results from a multinational trial. Dement Geriatr Cogn Disord 1999; 10: 237–244.
13. Rogers S, Friedhoff L, and the Donepezil Study Group. The efficacy and safety of Donepezil in patients with Alzheimer's disease: results of a US multicentre, randomized, double-blind, placebo-controlled trial. Dementia 1996; 7: 293–303.
14. Corey–Bloom J, Anand R, Veach J, for the ENA 713 B352 Study Group. A randomized trial evaluating the efficacy and safety of ENA 713 rivastigmine tartrate), a new acetylcholinesterase inhibitor, in patients with mild to moderately severe Alzheimer's disease. Int J Geriatr Psychopharmacol 1998; 1: 55–65.
15. Forette F, Anand R, Gharabawi G. A phase II study in patients with Alzheimer's disease to assess the preliminary efficacy and maximum tolerated dose of Rivastigmine (Exeloninfinity). Eur J Neurol 1999; 6: 423–429.

16. Rosler M, Anand R, Cicin–Sain A, et al. Efficacy and safety of Rivastigmine in patients with Alzheimer's disease: international randomised controlled trial. B Med J 1999; 318: 633–638.
17. Raskind M, Peskind E, Wessel T, et al. and the Galantamine Study Group. Galantamine in AD. A 6-month randomized, placebo-controlled trial with a 6-month extension. Neurology 2000; 54: 2261–2268.
18. Tariot P, Solomon P, Morris J, et al. and the Galantamine Study Group. A 5-month, randomized, placebo-controlled trial of galantamine in AD. Neurology 2000; 54: 2269–2276.
19. Thal L, Schwartz G, Sano M, et al. A multicenter double-blind study of controlled-release physostigmine for the treatment of symptoms secondary to Alzheimer's disease. Neurology 1996; 47: 1389–1395.
20. Thal L, Ferguson J, Mintzer J, et al. A 24-week randomized trial of controlled-release physostigmine in patients with Alzheimer's disease. Neurology 1999; 52: 1146–1152.
21. Cummings J, Cyrus P, Bieber F, et al. and the Metrifonate Study Group. Metrifonate treatment of the cognitive deficits of Alzheimer's disease. Neurology 1998; 50: 1214–1221.
22. Morris J, Cyrus P, Orazem J, et al. Metrifonate benefits cognitive, behavioral, and global function in patients with Alzheimer's disease. Neurology 1998; 50: 1222–1230.
23. Becker R, Colliver J, Markwell S, et al. Double-blind, placebo-controlled study of metrifonate, an acetylcholinesterase inhibitor, for Alzheimer's disease. Alzheimer Dis Assoc Disord 1996; 10: 124–131.
24. Zemlan F, Keys M, Richter R, et al. Double-blind placebo-controlled study of velnacrine in Alzheimer's disease. Life Sci 1996; 58: 1823–1832.
25. Antuono PG, for the Mentane Study Group. Effectiveness and safety of velnacrine for the treatment of Alzheimer's disease. Arch Intern Med 1995; 155: 1766–1772.
26. Canal N, Imbimbo B, for the Eptastigmine Study Group. Clinical trials and therapeutics: relationship between pharmacodynamic activity and cognitive effects of eptastigmine in patients with Alzheimer's disease. Clin Pharmacol Ther 1996; 60: 218–228.
27. Imbimbo B, Martelli P, Troetel W, et al. and the Eptastigmine Study Group. Efficacy and safety of eptastigmine for the treatment of patients with Alzheimer's disease. Neurology 1999; 52: 700–708.
28. Imbimbo B, Verdelli G, Martelli P, et al. and the Eptastigmine Study Group. Two-year treatment of Alzheimer's disease with eptastigmine. Dement Geriatr Cogn Disord 1999; 10: 139–147.
29. Heyman A, Schmechel D, Wilkinson W, et al. Failure of long-term high-dose lecithin to retard progression of early-onset Alzheimer's disease. J Neural Transm 1987; 24: 279–286.
30. Little A, Levy R, Chuaqui–Kidd P, et al. A double-blind, placebo controlled trial of high-dose Lecithin in Alzheimer's disease. J Neurol Neurosurg Psychiatry 1985; 48: 736–742.
31. Thal L, Forrest M, Loft H, et al. for the Lu25-109 Study Group. Lu25-109, a muscarinic agonist, fails to improve cognition in Alzheimer's disease. Neurology 2000; 25: 421–426.
32. Bodick N, Offen W, Levey A, et al. Effects of xanomeline, a selective muscarinic receptor agonist, on cognitive function and behavioral symptoms in Alzheimer's disease. Arch Neurol 1997; 54: 465–473.
33. Kumar R, Orgogozo J. Efficacy and safety of SB 202026 as a symptomatic treatment for Alzheimer's disease. In: Iqbal K, Winblad B, Nishimura T, Takeda M, and Wisniewski HM, eds. Alzheimer's disease: biology, diagnosis and therapeutics. New York: John Wiley & Sons, 1997:Chapter 85.
34. Jones G, Sahakian B, Levy R, et al. Effects of acute subcutaneous nicotine on attention, information processing and short-term memory in Alzheimer's disease. Psychopharmacology 1992; 108: 485–494.
35. Ruther E, Ritter R, Apecechea M, et al. Efficacy of the peptidergic nootropic drug cerebrolysin in patients with senile dementia of the Alzheimer type (SDAT). Pharmacopsychiatry 1994; 27: 32–40.
36. Soininen H, Koskinen T, Helkala E, et al. Treatment of Alzheimer's disease with a synthetic ACTH 4-9 analog. Neurology 1985; 35: 1348–1351.
37. Wolters E, Riekkinen P, Lowenthal A, et al. DGAVP (Org 5667) in early Alzheimer's disease patients: an international double-blind, placebo-controlled, multicenter trial. Neurology 1990; 40: 1099–1101.
38. Sourander L, Portin R, Molsa P, et al. Senile dementia of the Alzheimer type treated with Aniracetam: a new nootropic agent. Psychopharmacology 1987; 91: 90–95.
39. Cutler N, Shrotriya R, Sramek J, et al. The use of the computerized neuropsychological test battery (CNTB) in an efficacy and safety trial of BMY 21,502 in Alzheimer's disease. Ann N Y Acad Sci 1993; 695: 332–336.
40. Croisile B, Trillet M, Fondarai J, et al. Long-term and high-dose piracetam treatment of Alzheimer's disease. Neurology 1993; 43: 301–305.
41. Crook T, Petrie W, Wells C, et al. Effects of phosphatidylserine in Alzheimer's disease. Psychopharmacol Bull 1992; 28: 61–66.
42. Engel R, Satzger W, Günther W, et al. Double-blind cross-over study of phosphatidylserine vs. placebo in patients with early dementia of the Alzheimer type. Eur Neuropsychopharmacol 1992; 2: 149–155.
43. Fakouhi T, Jhee S, Sramek J, et al. Evaluation of cycloserine in the treatment of Alzheimer's disease. J Geriatr Psychiatr Neurol 1995; 8: 226–230.
44. Huff F, Antuono P, Delagandara J, et al. A treatment and withdrawal trial of besipirdine in Alzheimer's disease. Alzheimer Dis Assoc Disord 1996; 10: 93–102.
45. Dysken M, Mendels J, LeWitt P, et al. Milacemide: a placebo-controlled study in senile dementia of the Alzheimer type. J Am Geriatr Soc 1992; 40: 503–506.
46. Thompson T II, Filley C, Mitchell W, et al. Lack of efficacy of hydergine in patients with Alzheimer's disease. N Engl J Med 1990; 323: 445–448.
47. Thienhaus O, Wheeler B, Simon S, et al. A controlled double-blind study of high-dose dihydroergotoxine mesylate (hydergine) in mild dementia. J Am Geriatr Soc 1987; 35: 219–223.
48. Spagnoli A, Lucca U, Menasce G, et al. Long-term acetyl-L-carnitine treatment in Alzheimer's disease. Neurology 1991; 41: 1726–1732.

49. Thal L, Carta A, Clarke W, et al. A 1-year multicenter placebo-controlled study of acetyl-L-carnitine in patients with Alzheimer's disease. Neurology 1996; 47: 705–711.
50. Bergamasco B, Scarzella L, La Commare P. Idebenone, a new drug in the treatment of cognitive impairment in patients with dementia of the Alzheimer type. Funct Neurol 1994; 9: 161–168.
51. Weyer G, Babej–Dolle R, Hadler D, et al. A controlled study of two doses of idebenone in the treatment of Alzheimer's disease. Neuropsychobiology 1997; 36: 73–82.
52. Mangoni A, Grassi M, Frattola L, et al. Effects of a MAO-B inhibitor in the treatment of Alzheimer's disease. Eur Neurol 1991; 31: 100–107.
53. Freedman M, Rewilak D, Xerri T, et al. L-deprenyl in Alzheimer's disease: cognitive and behavioral effects. Neurology 1998; 50: 660–668.
54. Tollefson G. Short-term effects of the calcium channel blocker nimodipine (Bay-e-9736) in the management of primary degenerative dementia. Biol Psychiatry 1990; 27: 1133–1142.
55. Sano M, Ernesto C, Thomas RG, et al. A controlled trial of selegiline, alpha-tocopherol, or both as treatment for Alzheimer's disease. New Eng J Med 1997; 336: 1216–1222.
56. McGeer P, Schulzer M, McGeer E. Arthritis and anti-inflammatory agents as possible protective factors for Alzheimer's disease. Neurology 1996; 47: 425–432.
57. Rogers J, Kirby L, Hempelman S, et al. Clinical trial of indomethacin in Alzheimer's disease. Neurology 1993; 43: 1609–1611.
58. Scharf S, Mander A, Ugoni A, et al. A double-blind, placebo-controlled trial of diclofenac/misoprostol in Alzheimer's disease. Neurology 1999; 53: 197–201.
59. Aisen P, Davis K, Berg M, et al. A randomized controlled trial of prednisone in Alzheimer's disease. Neurology 2000; 54: 588–593.
60. Mulnard R, Cotman C, Kawas C, et al. Estrogen replacement therapy for treatment of mild to moderate Alzheimer's disease: a randomized, controlled trial. JAMA 2000; 283: 1007–1015.
61. Henderson V, Paganini–Hill A, Miller V, et al. Estrogen for Alzheimer's disease in women: randomized, double-blind, placebo-controlled trial. Neurology 2000; 54; 295–301.
62. Marcusson J, Rother M, Kittner B, et al. A 12-month, randomized, placebo-controlled trial of propentofylline (HWA 285) in patients with dementia according to DSM III-R. Dement Geriatr Cogn Disord 1997; 8: 320–328.
63. Moller H, Maurer I, Saletu B. Placebo-controlled trial of the xanthine derivative propentofylline in dementia. Pharmacopsychiat 1998; 27: 159–165.
64. Görtelmeyer R, Erbler H. Memantine in the treatment of mild to moderate dementia syndrome: a double-blind placebo-controlled study. Arzneim–Forsch/Drug Res 1992; 42: 904–913.
65. Ditzler K. Efficacy and tolerability of memantine in patients with dementia syndrome. Arzneim–Forsch/Drug Res 1991; 41: 773–780.
66. Villardita C, Parini J, Grioli S, et al. Clinical and neuropsychological study with oxiracetam versus placebo in patients with mild to moderate dementia. J Neural Transm 1987; 24: 293–298.
67. Villardita C, Grioli S, Lomeo C, et al. Clinical studies with oxiracetam in patients with dementia of Alzheimer type and multi-infarct dementia of mild to moderate degree. Neuropsychology 1992; 25: 24–28.
68. Bottini G, Vallar G, Cappa S, et al. Oxiracetam in dementia: a double-blind, placebo-controlled study. Acta Neurol Scand 1992; 86: 237–241.
69. Saletu B, Paulus E, Linzmayer L, et al. Nicergoline in senile dementia of Alzheimer type and multi-infarct dementia: a double-blind, placebo-controlled, clinical and EEG/ERP mapping study. Psychopharmacology 1995; 117: 385–395.
70. Battaglia A, Bruni G, Ardia A, et al. on behalf of the Italian Nicergoline Study Group. Nicergline in mild to moderate dementia: a multicenter, double-blind, placebo-controlled study. J Am Geriatr Soc 1989; 37: 295–302.
71. Fischhof P, Möslinger–Gehmayr R, Herrmann W, et al. Therapeutic efficacy of vincamine in dementia. Neuropsychobiology 1996; 34: 29–35.
72. Grossmann W, Standl A, May U, et al. Naftidrofuryl in the treatment of mild senile dementia: a double-blind study. Pharmacopsychiatry 1990; 23: 265–273.
73. Kanowski S, Fischhof P, Grobe–Einsler R, et al. Efficacy of xantinolnicotinate in patients with dementia. Pharmacopsychiatry 1990; 23: 118–124.
74. Olafsson K, Jorgensen S, Jensen HV, et al. Fluvoxamine in the treatment of demented elderly patients: a double-blind placebo-controlled study. Acta Psychiatr Scand 1992; 85: 453–456.
75. Le Bars P, Katz M, Berman N, et al. for the North American EGb Study Group. A placebo-controlled, double-blind, randomized trial of an extract of ginkgo biloba for dementia. JAMA 1997; 278: 1327–1332.
76. Kanowski S, Herrmann W, Stephan K, et al. Proof of efficacy of the ginkgo biloba special extract EGb 761 in outpatients suffering from mild to moderate primary degenerative dementia of the Alzheimer type or multi-infarct dementia. Pharmacopsychiatry 1996; 29: 47–56.
77. Wesnes K, Simmons D, Rook M, et al. A double-blind placebo-controlled trial of tanakan in the treatment of idiopathic cognitive impairment in the elderly. Human Psychopharmacol 1987; 2: 159–169.
78. Ban T, Morey L, Kfetland O, et al. Early manifestations of dementing illness: treatment with glycosaminoglycan polysulfate. Prog Neuropsychopharmacol Biol Psychiatry 1992; 16: 661–676.
79. Ban T, Morey L, Aguglia E, et al. Nimodipine in the treatment of old age dementias. Prog Neuropsychopharmacol Biol Psychiatry 1990; 14: 525–551.
80. Fischhof P, Saletu B, Rüther E, et al. Therapeutic efficacy of pyritinol in patients with senile dementia of the Alzheimer type (SDAT) and multi-infarct dementia (MID). Neuropsychobiology 1992; 26: 65–70.
81. Passeri M, Cucinotta D, Bonati P, et al. Acetyl-L-carnintine in the treatment of mildly demented elderly patients. Int J Clin Pharm Res 1990; 10: 75–79.

82. Maina G, Fiori L, Torta R, et al. Oxiracetam in the treatment of primary degenerative and multi-infarct dementia: a double-blind, placebo-controlled study. Neuropsychobiology 1989; 21: 141–145.
83. Albizatti M, Bassi S, Calloni E, et al. Cyclandelate vs. flunarizine: a double-blind study in a selected group of patients with dementia. Drugs 1987; 33: 90–96.
84. European Pentoxifylline Multi-Infarct Dementia (EPMID) Study Group. European Pentoxifylline Multi-Infarct Dementia study. Eur Neurol 1996; 36: 315–321.
85. Black R, Barclay L, Nolan K, et al. Pentoxifylline in cerebrovascular dementia. Am Geriatr Soc 1992; 40: 237–244.
86. Katz I, Jeste D, Mintzer J, et al and the Risperidone Study Group. Comparison of risperidone and placebo for psychosis and behavioral disturbances associated with dementia: a randomized, double-blind trial. J Clin Psychiatry 1999; 60: 107–115.
87. De Deyn P, Rabheru K, Rasmussen A, et al. A randomized trial of risperidone, placebo, and haloperidol for behavioral symptoms of dementia. Neurology 1999; 53: 946–955.
88. Street J, Clark W, Gannon K, et al. Olanzepine treatment of psychiatric and behavioral symptoms in patients with Alzheimer's disease in nursing care facilities: a double-blind, randomized, placebo-controlled trials. Arch Gen Psychiatry 2000 (in press).
89. Devanand D, Marder K, Michaels K, et al. A randomized, placebo-controlled dose-comparison trial of haloperidol for psychosis and disruptive behaviors in Alzheimer's disease. Am J Psychiatry 1998; 155: 1512–1520.
90. Frenchmen I, Prince T. Clinical experience with risperidone, haloperidol, and thioridazine for dementia-associated behavioral disturbances. Int Psychogeriatr 1997; 9: 431–435.
91. Coccaro E, Kramer E, Zemizhlany Z, et al. Pharmacologic treatment of non-cognitive behavioral disturbances in elderly demented patients. Am J Psychiatry 1990; 147: 1640–1645.
92. Gutzmann H, Kühl K, Kanowski S, et al. Measuring the efficacy of psychopharmacological treatment of psychomotoric restlessness in dementia: clinical evaluation of tiapride. Pharmacopsychiatry 1997; 30: 6–11.
93. McKeith I, Fairbairn A, Perry R, et al. Neuroleptic sensitivity in patients with senile dementia of Lewy body type. Br Med J 1992; 305: 673–678.
94. Saletu B, Hochmayer I, Grunberger J, et al. Zur therapie der multiinfarktdemenz mit Nicergolin 1): Doppelblinde, klinische, psychometrische und EEG-imainguntersuchungen mit 2 dosierungsschemata. WMW 1987; 32: 513–524.
95. McLachlan D, Smith W, Kruck T. Desferrioxamine and Alzheimer's disease: video home behavior assessment of clinical course and measures of brain aluminum. Ther Drug Monit 1993; 15: 602–607.
96. Tariot P, Erb R, Leibovici A, et al. Carbamazepine treatment of agitation in nursing home patients with dementia: a preliminary study. J Am Geriatr Soc 1994; 42: 1160–1166.
97. Nyth A, Gottfries C, Lyby K, et al. A controlled multicenter clinical study of citalopram and placebo in elderly depressed patients with and without concomitant dementia. Acta Psychiatr Scand 1992; 86: 138–145.
98. Reifler V, Teri L, Raskind M, et al. Double-blind trial of imipramine in Alzheimer's disease patients with and without depression. Am J Psychiatry 1989; 146; 45–49.
99. Petracca G, Teson A, Chemerinski E, et al. A double-blind placebo-controlled study of clomipramine in depressed patients with Alzheimer's disease. J Neuropsychiatry Clin Neurosci 1996; 8: 270–75.
100. Roth M, Mountjoy C, Amrein R, and the International Collaborative Study Group. Moclobemide in elderly patients with cognitive decline and depression. Br J Psychiatry 1996; 168: 149–157.
101. Fuchs A, Hehnke U, Erhart Ch, et al. Video rating analysis of effect of maprotiline in patients with dementia and depression. Pharmacopsychiatry 1993; 26: 37–41.
102. Taragano F, Lyketsos C, Mangone C, et al. A double-blind, randomized, fixed-dose trial of fluoxetine vs. amitriptyline in the treatment of major depression complicating Alzheimer's disease. Psychosomatics 1997; 38: 246–252.
103. Katona C, Hunter B, Bray J. A double-blind comparison of the efficacy and safety of paroxetine and imipramine in the treatment of depression with dementia. Int J Geriatr Psychiatry 1988; 13: 100–108.
104. Kahan J, Kemp B, Staples FR, et al. Decreasing the burden in families caring for a relative with a dementing illness: a controlled study. J Am Geriatr Soc 1985; 33: 664–670.
105. Hebert R, Grouard D, Leclerc G, et al. The impact of a support group programme for caregivers on the institutionalisation of demented patients. Arch Gerontol Geriatr 1995; 20: 129–134.
106. Brodaty H, Roberts K, Peters K. Quasi-experimental evaluation of an educational model for dementia caregivers. Int J Geriatr Psychiatry 1994; 9: 195–204.
107. Chiverton P, Caine E. Education to assist spouses in coping with Alzheimer's disease: a controlled trial. J Am Geriatr Soc 1989; 37: 593–598.
108. Brennan P, Moore S, Smyth K. The effects of a special computer network on caregivers of persons with Alzheimer's disease. Nurs Res 1995; 44: 166–172.
109. Brodaty H, Gresham M. Effect of a training programme to reduce stress in carers of patients with dementia. Br Med J 1989; 299: 1375–1379.
110. Mittelman M, Ferris S, Shulman E, et al. A family intervention to delay nursing home placement of patients with Alzheimer disease. JAMA 1996; 276: 1725–1731.
111. Ray W, Taylor J, Meador K, et al. Reducing antipsychotic drug use in nursing homes. Arch Intern Med 1993; 153: 713–721.
112. Tappen R. The effect of skill training on functional abilities of nursing home residents with dementia. Res Nurs Health 1994; 17: 159–65.
113. Coyne M, Hoskins L. Improving eating behaviors in dementia using behavioral strategies. Clin Nurs Res 1997; 6: 275–291.
114. Beck C, Heacock P, Mercer SO, et al. Improving dressing behavior in cognitively impaired nursing home residents. Nurs Res 1997; 46: 126–132.
115. McEvoy C, Patterson R. Behavioral treatment of deficit skills in dementia patients. Gerontologist 1986; 26: 475–478.
116. Zanetti O, Binetti G, Magni E, et al. Procedural memory stimulation in Alzheimer's disease: impact of a training programme. Acta Neurol Scand 1997; 95: 152–157.

117. Sixsmith A, Stilwell J, Copeland J. 'Rementia': challenging the limits of dementia care. Int J Geriatr Psychiatry 1993; 8: 993–1000.
118. Skelly J, Flint AJ. Urinary incontinence associated with dementia. J Am Geriatr Soc 1995; 43: 286–294.
119. Ouslander J, Schnelle J. Assessment, treatment and management of urinary incontinence in the nursing home. In: Rubenstein L, Wieland D, eds. Improving care in the nursing home: comprehensive review of clinical research. Newbury Park, CA: Sage Publications, 1993: 131–159.
120. Bach D, Bach M, Bohmer F, et al. Reactivating occupational therapy: a method to improve cognitive performance in geriatric patients. Age Ageing 1995; 24: 222–226.
121. Ford M, Fox J, Fitch S, et al. Light in the darkness. Nurs Times 1987; 83: 26–29.
122. Reichenback V, Kirchman M. Effects of a multi-strategy program upon elderly with organic brain syndrome. In: Taira ED, ed. The mentally impaired elderly. Binghamton, NY: Haworth Press, 1991: 131–151.
123. Hanley I, McGuire R, Boyd W. Reality orientation and dementia: a controlled trial of two approaches. Br J Psychiatry 1981; 138: 10–14.
124. Gerdner L. Effects of individualized versus classical "relaxation" music on the frequency of agitation in elderly persons with Alzheimer's disease and related disorders. Int Psychogeriatr 2000; 12: 49–65.
125. Tabloski P, McKinnon–Howe L, Remington R. Effects of calming music on the level of agitation in cognitively impaired nursing home residents. Am J Alzheimer's Care Related Disord & Res 1995 10–15.
126. Ragneskog H, Brane G, Karlsson I, et al. Influence of dinner music on food intake and symptoms common in dementia. Scand J Caring Sci 1996; 10: 11–17.
127. Cohen–Mansfield J, Werner P. Management of verbally disruptive behaviors in nursing home residents. J Gerontol 1997; 52A: M369–M377.
128. Clark M, Lipe A, Bilbrey M. Use of music to decrease aggressive behaviors in people with dementia. J Gerontol Nurs 1998;July:10–17.
129. Gerdner L, Swanson E. Effects of individualized music on confused and agitated elderly persons. Arch Psychiatr Nurs 1993; VII: 284–291.
130. Casby J, Holm M. The effect of music on repetitive disruptive vocalizations of persons with dementia. Am J Occup Ther 1994; 48: 883–889.
131. Thomas D, Heitman R, Alexander T. Effects of music on bathing cooperation for residents with dementia. J Music Ther 1997; 34: 246–259.
132. Denney A. Quiet music: an intervention for mealtime agitation? J Gerontolog Nurs 1997; 23: 16–23.
133. Camberg L, Woods P, Ooi W, et al. Evaluation of simulated presence: a personalized approach to enhance well-being in persons with Alzheimer's disease. J Am Geriatr Soc 1999; 47: 446–452.
134. Woods P, Ashley J. Simulated presence therapy: using selected memories to manage problem behaviors in Alzheimer's disease patients. Geriatr Nurs 1995; 16: 9–14.
135. Mishima K, Okawa M, Hishikawa Y, et al. Morning bright light therapy for sleep and behavior disorders in elderly patients with dementia. Acta Psychiatr Scand 1994; 89: 1–7.
136. Koss E, Gilmore G. Environmental interventions and functional ability of Alzheimer's disease patients. In: Vellas B, Fitten J, Frisoni G, eds. Research and practice in Alzheimer's disease. New York: Springer Publishing, 1998; 186–192.
137. Lovell B, Ancoli–Israel S, Gevirtz R. Effects of bright light treatment on agitated behavior in institutionalized elderly subjects. Psychiatr Res 1995; 57: 7–12.
138. Bourgeois M, Burgio L, Schulz R, et al. Modifying repetitive verbalizations of community-dwelling patients with AD. Gerontologist 1997; 37: 30–39.
139. Holmberg S. Evaluation of a clinical intervention for wanderers on a geriatric nursing unit. Arch Psychiatr Nurs 1997; XI: 21–28.
140. Namazi K, Gwinnup P, Zadorozny C. A low intensity exercise/movement program for patients with Alzheimer's disease: the TEMP-AD Protocol. J Aging Phys Activity 1994; 2: 80–92.
141. Brooker D, Snape M, Johnson E, et al. Single case evaluation of the effects of aromatherapy and massage on disturbed behavior in severe dementia. Br J Clin Psychol 1997; 36: 287–296.
142. Rowe M, Alfred D. The effectiveness of slow-stroke massage in diffusing agitated behaviors in individuals with Alzheimer's disease. J Gerontolog Nurs 1999;June:22–34.
143. Snyder M, Egan EC, Burns KR. Efficacy of hand massage in decreasing agitation behaviors associated with care activities in persons with dementia. Geriatr Nus 1995; 16: 60–63.
144. Rovner B, Steele C, Shmuely Y, et al. A randomized trial of dementia care in nursing homes [see comments]. J Am Geriatr Soc 1996; 44: 7–13.
145. Matteson M, Linton A, Cleary B, et al. Management of problematic behavioral symptoms associated with dementia: a cognitive developmental approach. Aging 1997; 9: 342–355.
146. Matthews E, Farrell G, Blackmore A. Effects of an environmental manipulation emphasizing client-centered care on agitation and sleep in dementia sufferers in a nursing home. J Adv Nurs 1996; 24: 439–447.
147. Lantz M, Buchalter E, McBee L. Wellness group: a novel intervention for coping with disruptive behavior in elderly nursing home residents. Gerontologist 1997; 37: 551–556.
148. Churchill M, Safaoui J, McCabe B, et al. Using a therapy dog to alleviate the agitation and desocialization of people with Alzheimer's disease. J Psychosoc Nurs 1999; 37: 16–22.
149. Hopman-Rock M, Staats P, Tak E, Droes R. The effects of a psychomotor activation programme for use in groups of cognitively impaired people in homes for the elderly. Int J Geriatr Psychiatry 1999; 14: 633–642.
150. Quayhagen M, Quayhagen M, Corbeil R, et al. A dyadic remediation program for care recipients with dementia. Nurs Res 1995; 44: 153–159.
151. Hart B, Wells D. Effects of language used by caregivers on agitation in residents with dementia. Clin Nurse Specialist 1997; 11: 20–23.

152. Robichaud L, Hebert R, Desrosiers J. Efficacy of a sensory integration program on behaviors of inpatients with dementia. Am J Occup Ther 1993; 355–360.
153. Wimo A, Nelvig A, Nelvig J, et al. Can changes in ward routines affect the severity of dementia? A controlled prospective study. Int Psychogeriatr 1993; 5: 169–180.
154. Sloane P, Mitchell C, Preisser J, et al. Environmental correlates of resident agitation in Alzheimer's disease special care units. J Am Geriatr Soc 1998; 46: 862–869.
155. Swanson E, Maas M, Buckwalter K. Catastrophic reactions and other behaviors of Alzheimer's residents: special unit compared with traditional units. Arch Psychiatr Nurs 1993; 7: 292–299.
156. Belleli G, Frisoni G, Bianchetti A, et al. Special care units for demented patients: a multicenter study. Gerontologist 1998; 38: 456–462.
157. Mintzer J, Colenda C, Waid L, et al. Effectiveness of a continuum of care using brief and partial hospitalization for agitated dementia patients. Psychiatr Serv 1435; 48: 1435–1439.
158. Volicer L, Collard A, Hurley A, et al. Impact of special care unit for patients with advanced Alzheimer's disease on patients' discomfort and costs. J Am Geriatr Soc 1994; 42: 597–603.
159. Mooney P, Nicell PL. The importance of exterior environment for Alzheimer residents: effective care and risk management. Healthcare Manage Forum 1992; 5: 23–29.
160. Mather J, Nemecek D, Oliver K. The effect of a walled garden on behavior of individuals with Alzheimer's. Am J Alzheimer's Dis 1997 252–257.
161. Cohen-Mansfield J, Werner P. The effects of an enhanced environment on nursing home residents who pace. Gerontologist 1998; 38: 199–208.
162. Whall A, Black M, Groh C, et al. Effects of natural environments upon agitation and aggression in late stage dementia patients. Am J Alzheimer's Dis 1997; 12: 216–220.
163. Annerstedt L, Gustafson L, Nilsson K. Medical outcome of psychosocial intervention in demented patients: one-year clinical follow-up after relocation into group living units. Int J Geriatr Psychiatry 1993; 8: 833–841.
164. Ostwald S, Hepburn K, Caron W, et al. Reducing caregiver burden: a randomized psychoeducational intervention for caregivers of persons with dementia. Gerontologist 1999; 39: 299–309.
165. Mittelman M, Ferris S, Shulman E, et al. A comprehensive support program: effect of depression in spouse-caregivers of AD patients. Gerontologist 1995; 35: 792–802.
166. Buckwalter K, Gerdner L, Kohout F, et al. A nursing intervention to decrease depression in family caregivers of persons with dementia. Arch Psychiatr Nurs 1999; 13: 80–88.
167. Hebert R, Leclerc G, Bravo G, et al. Efficacy of a support group programme for caregivers of demented patients in the community: a randomized controlled trial. Arch Gerontol Geriatr 1994; 18: 1–14.
168. Mohide E, Pringle D, Streiner D, et al. A randomized trial of family caregiver support in the home management of dementia. J Am Geriatr Soc 1990; 38: 446–454.
169. Lawton M, Brody E, Saperstein A. A controlled study of respite service for caregivers of Alzheimer's patients. Gerontologist 1989; 29: 8–16.
170. Flint A. Effects of respite care on patients with dementia and their caregivers. Int Psychogeriatr 1995; 7: 506–517.
171. Zarit S, Stephens M, Townsend A, et al. Stress reduction for family caregivers: effects of adult day care use. J Gerontol Soc Sci 1998; 53B: S267–S277.
172. Cefalu C, Ettinger W, Espeland M. A study of the characteristics of the dementia patients and caregivers in dementia-nonspecific adult day care programs. J Am Geriatr Soc 1996; 44: 654–659.
173. Perkins R, Poynton C. Group counseling for relatives of hospitalized presenile dementia patients: a controlled study. Br J Clin Psychol 1990; 29: 287–295.
174. Goodman C, Pynoos J. A model telephone information and support program for caregivers of Alzheimer's patients. Gerontologist 1990; 30: 399–404.
175. Marson D, Ingram K, Cody H, et al. Assessing the competency of patients with Alzheimer's Disease under different legal standards. A prototype instrument. Arch Neurol 1995; 52: 949–954.

Neurology®

Practice parameter: Management of dementia (an evidence-based review) [RETIRED]: Report of the Quality Standards Subcommittee of the American Academy of Neurology

R. S. Doody, J.C. Stevens, C. Beck, et al.

Neurology 2001;56;1154-1166
DOI 10.1212/WNL.56.9.1154

Practice parameter: Management of dementia (an evidence-based review) [RETIRED]: Report of the Quality Standards Subcommittee of the American Academy of Neurology

R. S. Doody, J.C. Stevens, C. Beck, et al.

Neurology 2001;56;1154-1166
DOI 10.1212/WNL.56.9.1154