Screening for Dementia: A Review of the Evidence

By

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Structured Abstract

Purpose: To review the evidence concerning screening for dementia syndrome (hereafter, dementia) in primary care settings to support recommendations from the US Preventive Services Task Force (USPSTF).

Data Sources: We searched MEDLINE, PsychINFO, EMBASE, and the Cochrane Collaboration Library from January 1994 to November 2001, with all searches limited to English language studies.

Study Selection: We developed an analytic framework and key questions concerning dementia screening and treatment to guide our search. We developed inclusion and exclusion criteria for each key question. For questions of prevalence or accuracy of screening tests, we required cross-sectional or cohort studies in a primary care population with an acceptable reference standard for diagnosis. For questions of treatment, we included randomized controlled trials (RCTs) of subjects with mild to moderate dementia.

Data Extraction: Two reviewers agreed on studies meeting inclusion and exclusion criteria and graded them according to USPSTF criteria. They then extracted data from included studies of fair to good quality and entered the data into evidence tables.

Data Synthesis: The prevalence of dementia increases with age and affects 25% to 47% of people age 85 years and older. More than one-half of patients with dementia in primary care practices are undiagnosed. We found no RCT of screening for dementia. The Mini-Mental Status Examination (MMSE) is a brief screening tool with clinically acceptable reliability and accuracy. Although no effective treatment has yet been documented for early vascular dementia, cholinesterase inhibitors slow the rate of cognitive decline in people with mild to moderate Alzheimer's disease with mild adverse effects. Antidepressant medication is effective in...
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reversing depressive symptoms in early dementia, but medical treatment of other behavioral and mood symptoms in early dementia is poorly studied. Intensive multi-component interventions for caregivers may delay nursing home placement and decrease caregiver burden, but they do not affect patients' health outcomes. Other benefits of screening and the potential harm of labeling have not been studied.

**Conclusion:** Screening tests can detect undiagnosed dementia and cholinesterase inhibitors effectively slow the rate of cognitive decline in people with mild to moderate Alzheimer's disease. The effect of these drugs or other treatments on people with dementia detected by screening is uncertain.
Introduction

Dementia is an acquired syndrome of decline in memory and at least one other cognitive domain, such as language, visuo-spatial, or executive function sufficient to interfere with social or occupational functioning in an alert person(1). Multiple diseases can cause the dementia syndrome (hereafter, dementia). Alzheimer’s disease and cerebrovascular ischemia are the two most common causes. Although such potentially reversible causes as hypothyroidism or vitamin B12 deficiency are often considered causes of dementia, no more than 1.5% of cases of mild to moderate dementia are fully reversible(2).

Age is the best studied and the strongest risk factor for dementia. Other risk factors for Alzheimer’s disease include having a first-degree relative with a history of Alzheimer’s disease, the apolipoprotein E-4 genotype, or a previous history of head trauma(3-5). Cardiovascular risk factors such as hypertension are associated with an increased risk of both Alzheimer’s disease and vascular dementia(3;6;7).

The aging of the US population has been accompanied by a dramatic rise in the prevalence of dementia. From 3% to 11% of persons over age 65 and 25% to 47% of those over age 85 have dementia(8-13). In 1997, the number of people with Alzheimer’s disease in the United States was estimated to be 2.3 million, more than 90% of whom were ages 60 years and older(14).

Dementia causes a high burden of suffering for patients, their families, and society(15;16). For patients, it leads to increased dependency and falls, and complicates other comorbid conditions. For families, it leads to anxiety, depression, and increased time in caring for a loved one. The annual societal cost of dementia is approximately $100 billion, from health care and related costs as well as lost wages for patients and family caregivers(10;17).
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Clinicians using routine history and physical examination do not readily diagnose dementia during clinic visits. More than 50% of people with dementia have never been diagnosed by a physician (18-22). This raises the possibility that screening tests might be able to identify people with undiagnosed dementia, to permit more patients to receive treatment and to deliver treatment at an earlier stage in the disease process. Given the low prevalence of reversible causes, a recommendation for screening will depend on evidence of benefits for persons with irreversible causes, primarily Alzheimer's disease and vascular dementia.

For dementia screening to lead to improved health outcomes, primary care providers would need to have a brief, accurate screening test to apply during routine office visits. A positive screening test would then result in an in-depth diagnostic interview and clinical examination performed by either the primary physician or a specialist such as a geriatrician or neurologist trained in the diagnosis of dementia. Finally, effective treatment would be available for many people diagnosed with dementia that would improve health outcomes. Ideal evidence for dementia screening would come from a randomized controlled trial (RCT) of a screening intervention with long-term follow-up for both adverse and beneficial effects of screening.

The 1996 Guide to Clinical Preventive Services from the US Preventive Services Task Force (USPSTF) found insufficient evidence to recommend either for or against screening (23). Since the last USPSTF review, several studies have been published concerning both pharmacologic and caregiver interventions. Given the new evidence and the large and growing importance of this condition, the RTI-University of North Carolina Evidence-based Practice Center (RTI-UNC EPC) conducted a systematic review of the literature regarding the benefits and the harms of screening primary care populations to detect undiagnosed cases of dementia.
Methods

Using USPSTF methods (24), we developed an analytic framework and key questions to guide our systematic review of the evidence for dementia screening. We searched first for studies of screening that provided direct evidence that screening improves cognitive, social, or physical function; number of hospitalizations, institutionalizations, or health care visits; behavioral problems; caregiver burden; accidental injury such as falls or automobile crashes; and patients’ overall health-related quality of life. We next searched for indirect evidence of the benefit of screening, the prevalence of undiagnosed dementia, the accuracy of screening tests, and the efficacy of pharmacologic treatment and nonpharmacologic interventions for Alzheimer’s disease and vascular dementia. We also searched for evidence of the adverse effects of screening and treatment.

We developed inclusion and exclusion criteria for selecting the evidence relevant to answer the key questions. Table 1 lists these criteria and the number of articles found meeting them for each question. We used the inclusion and exclusion criteria to develop search terms, and searched MEDLINE, PsychINFO, EMBASE, and Cochrane Library databases for systematic reviews and high-quality studies relevant to each question. We limited all searches to reviews and studies published in the English language between January 1, 1994, and November 5, 2001, with information relevant for a primary care population.

At least 2 authors reviewed abstracts and articles to identify those that met the inclusion criteria and then abstracted relevant information using standardized abstraction forms. We graded the articles using criteria developed by the USPSTF Methods Work Group (24). The authors worked closely with 2 members of the USPSTF throughout the review, periodically presenting reports to the full USPSTF. We distributed a draft systematic evidence review for
external peer review by experts in the field and relevant professional organizations and federal agencies and made revisions based on the feedback.

A more complete account of the methods of this review is available in the Appendix on the *Annals of Internal Medicine* website(25). The complete evidence review is available on the AHRQ website(2).

**Results**

**How Common is Undiagnosed Dementia?**

Three studies in primary care populations ages 65 years and older compared the frequency of dementia by standard diagnostic tests with medical record notation of dementia or cognitive impairment(21;22;26). From 3.2% to 12% of all patients met criteria for dementia but had no dementia documentation (Table 2). A population-based study found that the prevalence of undiagnosed dementia among individuals ages 65 years and older was 1.8%(27).

Undiagnosed patients accounted for 50% to 66% of all cases of dementia in the primary care populations studied. In one small study, 78.6% (11/14) of people with mild dementia, 71.4% (5/7) with moderate dementia, and 20% (1/5) with severe dementia had no medical record documentation(22). New screening testing in primary care practice could, therefore, double the number of patients diagnosed with dementia, and most newly discovered cases would have mild to moderate disease.

**How Accurate are the Screening Tests?**

The most widely used and studied screening test for dementia is the Mini-Mental State Examination (MMSE), a 30-point structured examination that can be completed in 5 to 10
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8

minutes in a clinical encounter(28). The test has reasonable reliability(28;29), but it requires reading, writing, and mathematics, and thus must be adjusted for educational status(30-35).

MMSE scores below 26 have been shown to correlate with development of clinical dementia within the next 3 to 6 years; a score of 25 has a likelihood ratio (LR) of 2.30 and a score of 24 has a LR of 2.45(36). At these cutpoints (i.e., 24 to 26), population-based studies in Canada have found the sensitivity of the MMSE to be between 70% and 86% with a specificity of 77% to 82%(29;37). If the MMSE were used to screen a population with a prevalence of undiagnosed dementia of 10%, about one-third of people with a positive screening test would actually have dementia on further diagnostic testing. This proportion declines when the MMSE is used in groups with a lower prevalence of dementia.

Several other screening tests have been proposed (the Clock-Drawing Test, the Modified Mini-Mental State Examination, the Mini-Cog, and the Instrumental Activities of Daily Living [IADL] score), including some that are less dependent than the MMSE on educational status. None, however, is as well studied or has been shown to be consistently superior to the MMSE in the general population. Testing for genetic mutations is a new approach that requires further study.

How Effective is Treatment for Mild to Moderate Vascular Dementia?

Although antihypertensive treatment reduces the development of stroke, the evidence is limited that similar treatment of people with mild to moderate vascular dementia prevents further progression of the dementia(38). One systematic review found no effect of aspirin on cognitive symptoms in people with vascular dementia(39).
Because autopsy studies found that acetylcholine is depleted in the brains of people with Alzheimer's disease, several research teams have studied cholinesterase inhibitors for their efficacy in improving cognition and function in these people. The Food and Drug Administration has approved 4 cholinesterase inhibitors for use in Alzheimer's disease.

Thirteen well-conducted RCTs and systematic reviews met our inclusion criteria. They examined the effects of cholinesterase inhibitors on people with mild to moderate Alzheimer's disease (apparently detected clinically rather than by screening) (Table 3) (40-52). Nearly all found a statistically significant difference in cognitive function between drug and placebo groups after 6 to 12 months. This difference manifests as a reduced rate of cognitive decline, as opposed to an improvement, in people taking cholinesterase inhibitors compared with those taking placebo.

After 6 to 12 months of treatment, the magnitude of the difference between the cholinesterase inhibitor and placebo groups is 4% to 6% on cognitive function scales. The usual annual decline in cognition on research measurement scales for people with mild to moderate Alzheimer's disease is 7% for mild dementia and 10% to 15% for moderate dementia(53;54). In addition to its effects on cognition, cholinesterase inhibitors stabilized or slightly improved a scale of clinician global impression of change after 6 to 12 months of treatment.

The evidence is mixed about the effects of cholinesterase inhibitors on functional measures such as IADLs. In general, the studies show an uncertain reduction in functional decline after 6 months of treatment but a statistically significant difference from placebo after 12 months of treatment(55-59). The difference in function between treatment and placebo groups is small, approximately 1% to 3%. The most positive study was a 12-month RCT of donepezil
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treatment of 431 community-dwelling people with mild to moderate Alzheimer’s disease. The investigators found a median time to clinically evident decline of 6.9 months in the placebo group and 11.9 months in the donepezil group(50;60).

Research has found no clinically important differences between people taking cholinesterase inhibitors and those taking placebo in the development of behavioral symptoms, although not all trials measure this important health outcome. No studies have reported results for more than 12 months of treatment, and studies rarely address other important health outcomes such as utilization of health care services, injuries, and caregiver burden.

How Effective are Other Medications for People with Mild to Moderate Alzheimer’s Disease?

The evidence is weak that drugs other than cholinesterase inhibitors are beneficial in people with Alzheimer’s disease. Several RCTs have examined the effects of ginkgo biloba on cognitive function in people with mild to moderate dementia. Two meta-analyses of these studies, including one that examined only the four highest quality studies, found an approximate 3% difference in cognitive scales between ginkgo biloba and placebo groups(61;62). A recent Cochrane review of 15 placebo-controlled studies found that selegiline, a selective monoamine oxidase inhibitor, produced a small improvement on cognitive testing, mood, and behavior but no improvement in global clinical ratings(63). The evidence that selegiline affects other health outcomes is limited. A 2-year RCT also examined the effect of vitamin E in people with moderate Alzheimer’s disease(64). The investigators found that vitamin E had no effect on cognition but limited evidence that it delayed institutionalization. No other well-conducted RCTs have examined the effects of vitamin E. Two recent well-conducted RCTs examined estrogen therapy for women with mild to moderate dementia(65;66). After 15 months, the study found no difference between estrogen and placebo groups.
How Effective are Neuroleptics in Treating Behavioral Problems Associated with Mild To Moderate Dementia Syndrome?

A potential benefit of early detection of dementia is that problem behaviors associated with psychotic symptoms could be recognized and treated with neuroleptics. Although RCTs have examined these agents in people with more severe dementia, no study has examined this treatment in patients with mild to moderate dementia who would be detected by screening.

How Effective are Antidepressants in People with Mild to Moderate Dementia?

Many people with mild to moderate dementia are depressed. Two RCTs provided evidence that antidepressants are effective for depressive symptoms among community-dwelling elderly persons with mild to moderate Alzheimer’s disease. One RCT with a crossover design showed that 6 weeks of therapy with clomipramine (a tricyclic antidepressant) reduced depressive symptoms (55); in a recent study, Lyketsos et al. found that sertraline effectively treated depression in individuals with both Alzheimer’s disease and major depression (58). The evidence is limited concerning the effects of antidepressants on cognition; no high-quality trial has examined other important health outcomes such as functional status, health-related quality of life, or clinician global clinical impression of change.

How Effective are Nonpharmacologic Interventions for People with Mild to Moderate Dementia?

Nonpharmacologic interventions for dementia include behavioral training, caregiver education, and supportive services. Nonpharmacologic interventions may be directed at either patients or their caregivers. Numerous studies of patient-directed interventions have targeted patients with severe dementia; no studies have targeted people with mild to moderate dementia.
Several well-conducted RCTs (67-72) and 1 systematic review (73) have examined nonpharmacologic interventions directed at caregivers of people with mild to moderate dementia (Table 4). Caregiver interventions are complex and varied but usually include 1 or more of the following components: support groups, individual or family counseling, skills training, or education. Caregiver interventions were studied for benefit to patient health outcomes and for evidence of benefit to caregivers themselves.

A systematic review found no significant differences in caregiver burden between intervention and control groups and concluded that little or no evidence exists that interventions to support caregivers of people with Alzheimer's disease yield quantifiable benefit (73). Two other RCTs had similar findings (67-69), while another 2 found modest benefits (71;74). The two positive studies involved multi-component interventions that reduced caregiver burden (67;69).

One of these positive RCTs found that a multi-component caregiver intervention also improved the functional status of care recipients, although the magnitude of this improvement is unclear (71). Two other studies found that intensive, comprehensive caregiver interventions enabled caregivers to maintain the affected persons at home for a substantially longer period of time (between 11 and 19 months) than those who did not receive the intervention (75;76).

**Does Knowledge of a Dementia Diagnosis Improve Patient and Family Planning for Future Medical Care and Safety?**

Individuals identified with early dementia by screening may have the opportunity to discuss the nature of the syndrome, its prognosis, and future planning in regard to health care, safety, and finances. They may be able to formulate advance directives, choose a person to exercise power of attorney for financial and personal care decisionmaking, consent to participate in research, and contemplate issues such as motor vehicle driving, self-neglect, financial victimization, and housing relocation. It may also permit earlier and more effective
administration of medication for co-existing conditions by improving medication adherence and avoiding drug interactions. No high-quality study has been done to verify, quantify, or refute these potential benefits.

What are the Adverse Effects of Screening and Early Treatment of Dementia?

The harms of dementia screening have not been systematically studied. Potential harms include risk of depression and anxiety, the time and cost of screening, and possible labeling effects. Relatively few physicians have received sufficient training in the diagnostic skills required to diagnose dementia and its causes. Patients and families may face long delays after a positive screen before they can obtain a reference standard diagnostic work-up. Once a diagnosis of dementia is given, the patient will be unlikely to qualify for long-term care insurance or acceptance into a continuous care retirement community. However, in surveys of elderly patients and caregivers of Alzheimer’s patients, most participants wanted to be told the diagnosis of dementia(77;78).

The harms of treatment apply primarily to drugs, both cholinesterase inhibitors and others. Common side effects experienced by people taking cholinesterase inhibitors are nausea, vomiting, weight loss, and diarrhea.

In the trials of galantamine, the dropout rate attributable to adverse events in participants ranged from 2% to 15% more in the drug group than the placebo group. In the trials of rivastigmine, the adverse effect rate was from 5% to 20% higher. In trials of higher dose (10 mg) donepezil, the adverse effect rate was about 8% higher. Tacrine has significant gastrointestinal and hepatic side effects. The odds ratio for dropout because of adverse events among people who took tacrine is 5.7 (95% confidence interval; 4.1 - 7.9.). In RCTs of other
drugs, dropout rates did not differ significantly between people who took gingko biloba, selegilene, or vitamin E and those who took placebo.

Discussion

The prevalence of dementia increases rapidly in the seventh and eighth decades of life; the condition affects 25% to 47% of people over age 85. Patients suffer from progressive cognitive and functional dependence, psychotic and depressive symptoms, and injuries. The burden of disease also extends to the caregivers, who have high rates of emotional and financial stress and depression. Among all primary care patients over age 65 who have dementia, one-half are undiagnosed.

No randomized trial has evaluated the overall efficacy of dementia screening in primary care. The MMSE is the best-studied brief screening tool for dementia. A cutpoint of 24 to 26 out of 30 points is usually accepted as a positive screen. At this cutpoint, the MMSE can identify cases of dementia with a sensitivity of 70% to 86% and specificity of 77% to 82%. Among the problems with this test are that scores must be adjusted for educational attainment and that the specificity is low enough that many people who test positive do not have dementia.

Cholinesterase inhibitor treatment of people clinically detected with mild to moderate Alzheimer's disease results in modest but consistent improvements in cognition and clinician global impression of change scores. Little evidence exists for the effectiveness of antihypertensives or aspirin for vascular dementia.

Limited evidence indicates that intensive, multi-component interventions to support caregivers may delay nursing home placement for people with Alzheimer's disease, but they have demonstrated few direct benefits for either patient or caregiver. Further benefits of
screening, including individual and family planning and better decisions about health care
interventions for other conditions, have not been studied.

The harms of dementia screening have not been systematically studied. Potential harms
include risk of depression and anxiety, the time and cost of screening, and possible labeling
effects.

Limitations of this Review

First, we did not include studies of mild cognitive impairment (MCI), a newly recognized
condition that progresses to dementia in approximately 15% of patients. Any screening program
is likely to identify many older patients with MCI, but its natural history and response to
treatment remain uncertain(79;80). Second, we limited our search to English language articles
and thus may have excluded studies from relevant non-English speaking populations. However,
we believe that our review successfully captured all studies that met inclusion criteria.

Future Research Needs

Important gaps remain in the current research on screening and treatment of dementia.
An RCT of screening for dementia in primary care with prospective evaluation of multiple health
outcomes would provide the best evidence for or against dementia screening. Given the high
prevalence of undiagnosed dementia among primary care patients over age 65 and the efficacy of
cholinesterase inhibitor treatment for clinically treated mild to moderate Alzheimer’s disease, a
trial of screening is justifiable. Such a trial should also monitor costs and harms and include the
effects of screening and treatment on cognition, function, health care utilization, health-related
quality of life, and caregiver burden.
The MMSE has been criticized for limited specificity and the need to adjust scoring for age and educational attainment. Future research should examine other promising brief screening tools that may be less education-dependent, testing their positive and negative predictive value in primary care. Although caregiver burden, increased health care utilization, problem behaviors, psychiatric symptoms, and accidental injury are common in dementia, little work to date has dealt with treatments to reduce these important aspects of the syndrome. The design of nonpharmacologic interventions might be refined to target specific outcomes, such as problem behaviors or effective advance planning for health care decisions and safety. No RCT has yet evaluated the efficacy of nonpharmacologic interventions on behavioral symptoms in patients with screen-detected mild to moderate dementia who live at home; this may be another important direction for research.

Future pharmacologic treatment trials should routinely measure outcomes in addition to cognition and global clinical impression of change scores, including functional status, problem behaviors, and caregiver burden. In addition, outcome measures should be reported in temporal units such as time to decline or survival analyses, to provide data on stabilization of the disease course.

Dementia after age 65 is common and creates significant suffering for patients and family caregivers. Routine clinical visits to primary care providers leave most cases of dementia undiagnosed, but a brief clinical screening test can improve case detection. Strong evidence supports the use of cholinesterase inhibitors to slow modestly the rate of cognitive decline in people with clinically detected Alzheimer's disease. Their effectiveness in screening-detected Alzheimer's disease is less certain. Potential benefits of screening could increase with the discovery of more effective treatment for early, screening-detected Alzheimer's disease and vascular dementias.
### Table 1. Key Issues, Inclusion Criteria, and Number of Articles Meeting Criteria

<table>
<thead>
<tr>
<th>Issue</th>
<th>Inclusion Criteria</th>
<th>Number of Systematic Reviews and Articles Meeting Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>Published between 1/1/94 and 11/5/01</td>
<td>Studies - 4</td>
</tr>
<tr>
<td></td>
<td>English language</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Human subjects, age 60+</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MEDLINE, PsychINFO, EMBASE, Cochrane Library</td>
<td></td>
</tr>
<tr>
<td>Prevalence of undiagnosed dementia</td>
<td>Systematic reviews Cross-sectional prevalence</td>
<td>Systematic review - 1</td>
</tr>
<tr>
<td></td>
<td>Community or primary care setting</td>
<td>Studies - 11</td>
</tr>
<tr>
<td></td>
<td>Appropriate reference standard</td>
<td></td>
</tr>
<tr>
<td>Accuracy of screening tools</td>
<td>Systematic reviews; RCTs</td>
<td>Systematic review - 1</td>
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<tr>
<td></td>
<td>Prospective cohort</td>
<td>Studies - 11</td>
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<tr>
<td></td>
<td>Cross-sectional</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Community or primary care setting</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Appropriate reference standard</td>
<td></td>
</tr>
<tr>
<td>Treatment for vascular dementia</td>
<td>Systematic reviews, RCTs</td>
<td>Systematic review - 1</td>
</tr>
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<td></td>
<td>Mild to moderate dementia</td>
<td>Study - 1</td>
</tr>
<tr>
<td></td>
<td>Health outcomes</td>
<td></td>
</tr>
<tr>
<td>Pharmacologic interventions</td>
<td>Systematic reviews, RCTs</td>
<td>Studies - 19</td>
</tr>
<tr>
<td></td>
<td>Mild to moderate dementia</td>
<td></td>
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<tr>
<td></td>
<td>Health outcomes</td>
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</tr>
<tr>
<td>Nonpharmacologic interventions</td>
<td>Systematic reviews, RCTs</td>
<td>0</td>
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<tr>
<td></td>
<td>Mild to moderate dementia</td>
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</tr>
<tr>
<td></td>
<td>Health outcomes</td>
<td></td>
</tr>
<tr>
<td>Interventions for planning</td>
<td>Systematic reviews, RCTs</td>
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<tr>
<td></td>
<td>Mild to moderate dementia</td>
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<tr>
<td></td>
<td>Health outcomes</td>
<td></td>
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<tr>
<td>Caregiver interventions</td>
<td>Systematic reviews, RCTs</td>
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<td>Mild to moderate dementia</td>
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<td>Harms of screening</td>
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<td></td>
<td>Mild to moderate dementia</td>
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<tr>
<td></td>
<td>Psychological or other health outcomes</td>
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Table 2. Estimates of Undiagnosed Dementia in Primary Care Practices

<table>
<thead>
<tr>
<th>Study</th>
<th>Setting</th>
<th>Age of Patient Population</th>
<th>Reference Standard*</th>
<th>Prevalence of Missed Dementia in All Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olafsdottir et al., 2000(21)</td>
<td>Primary health center, Sweden</td>
<td>&gt; 70 years</td>
<td>DSM-III-R</td>
<td>12.0%</td>
</tr>
<tr>
<td>Eefsting et al., 1996(26)</td>
<td>Community and general practices, Netherlands</td>
<td>≥ 66 years</td>
<td>DSM-III</td>
<td>3.2%</td>
</tr>
<tr>
<td>Valcour, et al., 2000(22)</td>
<td>General internal medicine clinic, Hawaii</td>
<td>≥ 65 years</td>
<td>DSM-III-R</td>
<td>5.7%</td>
</tr>
<tr>
<td>Sternberg et al., 2000(27)</td>
<td>Community Medicine, Canada</td>
<td>≥ 65 years</td>
<td>DSM-III-R</td>
<td>1.8%</td>
</tr>
</tbody>
</table>

Table 3. Efficacy of Cholinesterase Inhibitors in Alzheimer's Disease

<table>
<thead>
<tr>
<th>Drug (Number of Trials)</th>
<th>Cognitive Function</th>
<th>Clinician-assessed Global Function</th>
<th>Physical Function: Activities of Daily Living (ADLs)</th>
<th>Behavioral Symptoms</th>
<th>Quality of Life</th>
<th>Caregiver Burden</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tacrine + (2)(40;46)</td>
<td>+</td>
<td>+</td>
<td>NS</td>
<td>NS</td>
<td>NT</td>
<td>NT</td>
</tr>
<tr>
<td>Donepezil + (5)(41;44;45;50;52)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>NS</td>
<td>NS</td>
<td>+</td>
</tr>
<tr>
<td>Rivastigmine + (2)(42;43)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>NS</td>
<td>NT</td>
<td>NT</td>
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<tr>
<td>Galantamine + (4)(47-49;51)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>NS</td>
<td>NT</td>
<td>NT</td>
</tr>
</tbody>
</table>

Key:

+: Statistically significant

NS: No significant effect

NT: Not tested
Table 4. Summary of Efficacy of Caregiver Interventions

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Patient Outcomes</th>
<th>Caregiver Outcomes</th>
<th>Time to Nursing Home Placement</th>
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</thead>
<tbody>
<tr>
<td>Mittleman et al., 1996(70)</td>
<td>NT</td>
<td>NT</td>
<td>+</td>
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<tr>
<td>Marriott et al., 2000(72)</td>
<td>NS</td>
<td>+</td>
<td>NT</td>
</tr>
<tr>
<td>McCurry et al., 1998(71)</td>
<td>NS</td>
<td>+</td>
<td>NT</td>
</tr>
<tr>
<td>Brodaty et al., 1997(76)</td>
<td>NT</td>
<td>NT</td>
<td>+</td>
</tr>
<tr>
<td>Hebert et al., 1994(67;69)</td>
<td>NS</td>
<td>NS</td>
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<tr>
<td>Hebert et al., 1995(69)</td>
<td>NS</td>
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</tr>
</tbody>
</table>

Key:
+ : Statistically significant
NS: No significant effect
NT: Not tested
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(29) McDowell, I., Kristjansson, B., Hill, G. B., and Hebert, R. Community screening for dementia: the Mini Mental State Exam (MMSE) and Modified Mini-Mental State Exam (3MS) compared. J Clin Epidemiol 50(4), 377-383. 97.


(41) Burns A, Rossor M, Hecker J, Gauthier S, Petit H, Moller H et al. The effects of


