Malaz Boustani, MD, MPH; Britt Peterson, MD, MPH; Laura Hanson, MD, MPH; Russell Harris, MD, MPH; and Kathleen N. Lohr, PhD

Background: Dementia is a large and growing problem but is often not diagnosed in its earlier stages. Screening and earlier treatment could reduce the burden of suffering of this syndrome.

Purpose: To review the evidence of benefits and harms of screening for and earlier treatment of dementia.

Data Sources: MEDLINE, PsycINFO, EMBASE, the Cochrane Library, experts, and bibliographies of reviews.

Study Selection: The authors developed eight key questions representing a logical chain between screening and improved health outcomes, along with eligibility criteria for admissible evidence for each question. Admissible evidence was obtained by searching the data sources.

Data Extraction: Two reviewers abstracted relevant information using standardized abstraction forms and graded article quality according to U.S. Preventive Services Task Force criteria.

Data Synthesis: No randomized, controlled trial of screening for dementia has been completed. Brief screening tools can detect some persons with early dementia (positive predictive value ≤50%). Six to 12 months of treatment with cholinesterase inhibitors modestly slows the decline of cognitive and global clinical change scores in some patients with mild to moderate Alzheimer disease. Function is minimally affected, and fewer than 20% of patients stop taking cholinesterase inhibitors because of side effects. Only limited evidence indicates that any other pharmacologic or nonpharmacologic intervention slows decline in persons with early dementia. Although intensive multicomponent caregiver interventions may delay nursing home placement of patients who have caregivers, the relevance of this finding for persons who do not yet have caregivers is uncertain. Other potential benefits and harms of screening have not been studied.

Conclusions: Screening tests can detect undiagnosed dementia. In persons with mild to moderate clinically detected Alzheimer disease, cholinesterase inhibitors are somewhat effective in slowing cognitive decline. The effect of cholinesterase inhibitors or other treatments on persons with dementia detected by screening is uncertain.

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Dementia causes a high burden of suffering for patients, their families, and society (15–21). For patients, it leads to increased dependency and complicates other comorbid conditions. For families, it leads to anxiety, depression, and increased time spent caring for a loved one. The annual societal cost of dementia is approximately $100 billion (health care and related costs as well as lost wages for patients and family caregivers) (10, 16, 22).

Clinicians using routine history and physical examination do not readily diagnose dementia during clinic visits. More than 50% of persons with dementia, including many with mild but some with moderate dementia, have never received a diagnosis of dementia from a physician (23–27). This raises the possibility that screening tests might be able to identify persons with undiagnosed dementia and thereby permit patients and their families to receive care at an earlier stage in the disease process. Given the low prevalence of reversible causes of dementia, a recommendation for screening would depend on evidence of the additional benefits of earlier treatment for persons whose dementia has an irreversible cause, primarily Alzheimer disease and vascular dementia.

For dementia screening to lead to improved health outcomes, primary care providers would need a brief, accurate screening test that could be applied during routine office visits. A positive result could then lead to a diagnostic interview and clinical examination based on the Diagnostic and Statistical Manual of Mental Disorders, fourth
screening for dementia in primary care

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The accuracy of screening tests; the efficacy of early pharmacologic and nonpharmacologic treatment for persons with Alzheimer disease and vascular dementia; caregiver intervention for persons with dementia; and the efficacy of interventions targeted to caregivers. We also searched for evidence of the adverse effects of screening and treatment.

At least two authors reviewed abstracts and articles to identify those that met the eligibility criteria and then abstracted relevant information using standardized abstraction forms. We graded the quality of the included articles using USPSTF criteria (31). In all cases, we accepted single studies or systematic reviews that addressed the key questions, met eligibility criteria, and were rated to be at least fair quality. Table 1 lists these criteria and the number of articles that met them for each question. A more thorough account of the methods used in this review can be found in the Appendix (available at www.annals.org).

This evidence report was developed by the RTI–University of North Carolina Evidence-based Practice Center under contract to the Agency for Healthcare Research and Quality. Staff of the funding agency and members of the USPSTF contributed to the study design, reviewed draft and final manuscripts, and made editing suggestions.

RESULTS

The best evidence for or against screening for dementia would be derived from a well-designed RCT of screening with health outcomes. No such trial has been completed. In the absence of such a trial, evidence for or against screening comes from studies of the prevalence of undiagnosed dementia, the accuracy of screening instruments, the efficacy of treatments for persons with dementia detected by screening, and the harms of screening and treatment.

How Common Is Undiagnosed Dementia?

Three studies in primary care samples of patients 65 years of age and older compared dementia detected by using standard diagnostic tests with documentation of dementia or cognitive impairment in the medical record (26, 27, 32) or with dementia noted on independent physician questionnaires (27). Among all primary care patients 65 years of age and older, 3.2% to 12% met criteria for dementia without dementia documentation or physician knowledge of dementia (Table 2). A population-based study found that the prevalence of undiagnosed dementia among persons 65 years of age and older was 1.8% (33). Another population-based study found that approximately half of reliable relatives of men with mild dementia failed to recognize that the men had problems with thinking or memory (81).

Patients who had not received a dementia diagnosis accounted for 50% to 66% of all cases of dementia in the primary care samples studied. Most missed cases were mild to moderate. In one small study, 78.6% of persons with mild dementia (11 of 14), 71.4% of persons with moderate dementia (5 of 7), and 20% of persons with severe dementia (1 of 5) had no documentation of a dementia diagnosis in the medical record (27). New screening in primary care practice could therefore potentially double the number of...
patients who receive a diagnosis of dementia. Most newly detected cases would be mild to moderate.

How Accurate Are the Screening Tests?

Three methodologic problems make it difficult to assess the accuracy of screening tests for dementia. First, the accuracy of many screening instruments has been researched, but to a limited degree. Few instruments have been examined in more than two or three small studies. Second, investigators have used a variety of reference standards for the diagnosis of dementia. Because functions such as cognition are continuous, the reference standard must set the point at which dementia can be diagnosed. Where this point is set makes a large difference in evaluating screening tests (82). Although research has yet to determine the optimal point for diagnosing dementia, the DSM-IV criteria are widely accepted in the United States and will be used as the standard in this review (83). Third, the samples used in the studies of screening instruments varied greatly. Many studies included participants with severe dementia or persons from memory clinics, who are

Table 1. Key Questions, Eligibility Criteria, and Number of Articles Meeting Criteria*

<table>
<thead>
<tr>
<th>Key Question</th>
<th>Eligibility Criteria</th>
<th>Systematic Reviews (Reference)</th>
<th>Additional Studies Not in Systematic Reviews (Reference)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>Published 1 January 1994–1 September 2002 English language Human subjects age ≥60 y MEDLINE, PsycINFO, EMBASE, Cochrane Library</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1. Direct evidence of screening</td>
<td>RCT of screening Health outcomes</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2. Prevalence of undiagnosed dementia</td>
<td>Systematic reviews Cross-sectional prevalence Community or primary care setting Appropriate reference standard</td>
<td>0</td>
<td>4 (26, 27, 32, 33)</td>
</tr>
<tr>
<td>3. Accuracy of screening tests</td>
<td>Systematic reviews; prospective cohorts Cross-sectional prevalence Community or primary care setting Appropriate reference standard</td>
<td>1 (37)</td>
<td>9 (39–43, 45, 60, 61, 84)</td>
</tr>
<tr>
<td>5. Efficacy of nonpharmacologic interventions</td>
<td>Systematic reviews, RCTs Mild to moderate dementia Health outcomes</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>For patients</td>
<td>Systematic reviews, RCTs Mild to moderate dementia Health outcomes</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>For caregivers</td>
<td>Systematic reviews, RCTs Mild to moderate dementia Health outcomes</td>
<td>1 (53)</td>
<td>6 (54–59)†</td>
</tr>
<tr>
<td>6. Efficacy of interventions for planning</td>
<td>Systematic reviews, RCTs Mild to moderate dementia Health outcomes</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>7. Harms of screening</td>
<td>Systematic reviews, RCTs Mild to moderate dementia Psychological or other health outcomes</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>8. Harms of treatment</td>
<td>Systematic reviews, RCTs Mild to moderate dementia Health outcomes</td>
<td>4 (72–75)</td>
<td>5 (76–80)</td>
</tr>
</tbody>
</table>

* RCT = randomized, controlled trial.
† Two articles were combined because they both reported the results of one study.

Table 2. Estimates of Undiagnosed Dementia in Primary Care Practices*

<table>
<thead>
<tr>
<th>Study, Year (Reference)</th>
<th>Setting</th>
<th>Age of Patient Sample, y</th>
<th>Reference Standard</th>
<th>Prevalence of Undiagnosed Dementia in All Patients, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olafsdottir et al., 2000 (26)</td>
<td>Primary health center, Sweden</td>
<td>≥70</td>
<td>DSM-III-R</td>
<td>12</td>
</tr>
<tr>
<td>Eefsting et al., 1996 (32)</td>
<td>Community and general practices, the Netherlands</td>
<td>≥65</td>
<td>DSM-III</td>
<td>3.2</td>
</tr>
<tr>
<td>Valcour et al., 2000 (27)</td>
<td>General internal medicine clinic, Hawaii</td>
<td>≥65</td>
<td>DSM-III-R</td>
<td>5.7</td>
</tr>
<tr>
<td>Sternberg et al., 2000 (33)</td>
<td>General, randomly sampled community, Canada</td>
<td>≥65</td>
<td>DSM-III-R</td>
<td>1.8</td>
</tr>
</tbody>
</table>

* DSM-III = Diagnostic and Statistical Manual of Mental Disorders, third edition; DSM-III-R = Diagnostic and Statistical Manual of Mental Disorders, third edition, revised.
not the focus of screening. Few studies have provided information on the accuracy of screening tests for detecting mild dementia. Thus, the evidence on test accuracy from these studies may be most appropriately extrapolated to detection of moderate dementia, and these tests may be less accurate in detecting mild dementia. Although we examined many studies of screening tests, we included only those that examined instruments feasible for use in primary care settings, used DSM-IV (or similar) criteria as the reference standard, and provided information about the test’s characteristics among persons who were not known to have symptoms of dementia.

Most screening tests for dementia can be divided into cognitive tests of patients and functional assessments that use both patients and others as informants. In 1996, the Agency for Health Care Policy and Research published a systematic review and meta-analysis of studies that evaluated dementia screening tools (37). The review found one informant-based functional status instrument and four patient-based cognitive assessment tools (including the Mini-Mental Status Examination [MMSE], the most commonly used and studied screening test for dementia). The MMSE is most accurate for white persons with at least a high school education. One way of compensating for this is to change the cut-point for an abnormal test result for patients of different ages and education levels (104). Whether this approach or other patient-based cognitive screening tools will be able to overcome demographic-related variance in accuracy remains unclear.

The Functional Activities Questionnaire was the informant-based functional assessment tool examined by the Agency for Health Care Policy and Research study (Table 3). Few other high-quality studies have focused on functional assessments to screen for dementia. One promising screening test that warrants further study is the Informant Questionnaire on Cognitive Decline in the Elderly, which assesses change in cognitive function as well as activities of daily living (42).

In summary, some patient-based cognitive screening tests with reasonable accuracy for detecting mild to moderate dementia are available, and research continues on other instruments and approaches. Although the MMSE is the most widely used and studied screening test for dementia, it requires specific adjustment for age and education. Tests of functional assessment have promise but need further study.

Because the apolipoprotein E ε4 allele is found approximately three times more frequently in persons with Alzheimer disease than in those without this condition, some groups have expressed interest in testing for this allele to screen for dementia (105). Many people with Alzheimer disease, however, do not have the apolipoprotein E ε4 allele, and many who have the allele never develop dementia (5). The value of this test in screening for dementia has yet to be demonstrated.

**How Effective Are Pharmacologic Interventions for Persons with Mild to Moderate Dementia?**

To be effective, interventions for persons with dementia should ideally improve functional status to a degree discernible by caregivers or health care providers. Interpreting whether the change in an index of function in a clinical trial meets this criterion requires an understanding of measurement instruments for function as well as the natural history of Alzheimer disease. In most clinical research on Alzheimer disease, function is measured by one or both of two scales: the Alzheimer’s Disease Assessment Scale for Cognition (ADAS-Cog), a 70-point scale that measures cognitive status, and the Clinician’s Interview-Based Impression of Change (CIBIC), a scale that also includes caregiver input. The CIBIC includes information from patient

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**Table 3. Accuracy of Screening Tests for Dementia**

<table>
<thead>
<tr>
<th>Instrument (Reference)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE (37, 39–43, 84, 85)</td>
<td>71–92</td>
<td>56–96</td>
<td>15–72</td>
<td>95–99</td>
</tr>
<tr>
<td>FAQ (37)</td>
<td>90</td>
<td>90</td>
<td>50</td>
<td>99</td>
</tr>
<tr>
<td>BIMC (37, 84)</td>
<td>90</td>
<td>65–90</td>
<td>22–50</td>
<td>98–99</td>
</tr>
<tr>
<td>BOMC (37)</td>
<td>69</td>
<td>90</td>
<td>43</td>
<td>96</td>
</tr>
<tr>
<td>STMS (37)</td>
<td>81</td>
<td>90</td>
<td>47</td>
<td>98</td>
</tr>
</tbody>
</table>

* BIMC = Blessed Information Memory Concentration; BOMC = Blessed Orientation Memory Concentration; FAQ = Functional Activities Questionnaire; MMSE = Mini-Mental Status Examination; STMS = Short Test of Mental Status.

† Based on a dementia prevalence of 10%.
Table 4. Efficacy of Cholinesterase Inhibitors in Patients with Alzheimer Disease after 3 to 12 Months*

<table>
<thead>
<tr>
<th>Drug (Reference)</th>
<th>Patients, n</th>
<th>Effect on Cognitive Function as Assessed by the Mean Difference between Drug and Placebo Groups on the ADAS-Cog†‡</th>
<th>Range of Odds Ratio for Having Stable Global Function or Better after Drug Treatment Compared with Placebo, as Measured by the CIBIC†</th>
<th>Effect on Physical Function as Assessed by IADLs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tacrine (74)</td>
<td>1984</td>
<td>1.36–2.78</td>
<td>1.18–2.11</td>
<td>Inconclusive</td>
</tr>
<tr>
<td>Donepezil (73, 76, 77, 79, 80)</td>
<td>1980</td>
<td>2.12–3.01</td>
<td>2.04–2.63</td>
<td>Inconclusive</td>
</tr>
<tr>
<td>Rivastigmine (72, 78)</td>
<td>4095</td>
<td>2.28–2.4</td>
<td>1.4–2.36</td>
<td>Inconclusive</td>
</tr>
<tr>
<td>Galantamine (75)</td>
<td>1674</td>
<td>3.00–3.4</td>
<td>1.71–1.94</td>
<td>Inconclusive</td>
</tr>
</tbody>
</table>

* ADAS-Cog = Alzheimer’s Disease Assessment Scale for Cognition; CIBIC = Clinician’s Interview-Based Impression of Change; IADL = instrumental activity of daily living.
† All between-group differences were statistically significant.
‡ The values represent the range of differences in the ADAS-Cog between the treatment and placebo groups.

...and caregiver interviews conducted by an experienced and independent clinician. The clinician rates the patient on a 7-point scale in which 1 indicates very much better, 4 indicates no change, and 7 indicates very much worse. Both the ADAS-Cog and the CIBIC scales are stable and sensitive to clinical change over time (106).

The natural history of Alzheimer disease is one of progressive decline. Patients’ cognitive, physical, and social functions gradually deteriorate. Thus, “improvement” from an intervention for Alzheimer disease is defined as a slowed rate of decline. The rate of decline in Alzheimer disease is not linear, however (107). Persons with mild dementia experience an average rate of decline of 5 or fewer ADAS-Cog points (≤2 MMSE points) per year. Thus, for persons with mild dementia, slowing decline by 2 to 3 ADAS-Cog points over a year could mean a delay of up to 7 months in disease progression.

By contrast, persons with moderate dementia (ADAS-Cog score >15 but <55) experience an average decline in cognition of 7 to 11 ADAS-Cog points (2 to 4 MMSE points) annually (107–110). Thus, for persons with moderate dementia, slowing decline by 2 to 3 ADAS-Cog points per year could mean a delay of 2 to 5 months in disease progression. An average difference between intervention and control groups of 2 to 3 ADAS-Cog points could be attributed to this amount of delay in disease progression for all persons in the intervention group or to a longer delay in some persons and no delay in others. Clinically, a difference of 2 to 3 points on the ADAS-Cog (110) is equivalent to, for example, a person remembering who came to dinner the previous evening or performing familiar tasks, such as dressing (111).

Cholinesterase Inhibitors

Four systematic reviews (72–75) and five additional RCTs (76–80) compared one of the four U.S. Food and Drug Administration–approved cholinesterase inhibitors with placebo among persons with mild to moderate Alzheimer disease, apparently detected clinically. All nine studies were well conducted (Table 4). With few exceptions, all of these studies, which involved at least 6 months of follow-up, found a statistically significant difference between the drug and placebo groups that favored the cholinesterase inhibitor, ranging from 2.12 to 3.4 points on the ADAS-Cog scale. This difference manifests as a reduced rate of cognitive decline in persons taking cholinesterase inhibitors compared with those taking placebo.

In addition to their effects on cognition, cholinesterase inhibitors also stabilized or slightly improved clinical global impression of change as measured by the CIBIC after 6 to 12 months of treatment. In many studies, the proportion of patients whose condition had stabilized was an absolute 10% to 20% higher in the cholinesterase group than in the placebo group. The evidence is mixed, however, about the effects of cholinesterase inhibitors on functional measures such as instrumental activities of daily living (that is, ability to use the telephone, ability to use modes of transportation, ability to take responsibility for medication, and ability to handle finances). In general, the studies showed little or no effect on functional decline after 6 months of treatment and a small but statistically significant difference from placebo after 12 months of treatment (34–36, 38, 44). The most positive study was a 12-month RCT of donepezil treatment in 431 community-dwelling persons with mild to moderate Alzheimer 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 (90, 100).

Research has found no clinically important differences between persons taking cholinesterase inhibitors and those taking placebo in the development of behavioral and psychological symptoms, although not all trials measure this important health outcome. No well-conducted RCT of cholinesterase inhibitors has maintained a placebo-controlled, blinded control group for more than 12 months of treatment, and studies have rarely addressed other important health outcomes, such as utilization of health care services, injuries, and caregiver burden.

Ginkgo biloba, Selegiline, Vitamin E, and Estrogen

The evidence is weak that drugs other than cholinesterase inhibitors have important benefits for persons with Alzheimer disease. Several RCTs have examined the effects of Ginkgo biloba on cognitive function in persons 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 the *Ginkgo biloba* and placebo groups (16, 46).

A recent Cochrane review and meta-analysis of 15 placebo-controlled studies found that selegiline, a selective monoamine oxidase inhibitor, produced no clinically important differences in cognition, function, mood, behavior, or global clinical ratings when compared with placebo (47). In a 2-year RCT of the effect of vitamin E in persons with moderate Alzheimer disease, investigators concluded that it had no effect on cognition but found limited evidence that it delayed institutionalization (48). No other well-conducted RCT has examined the effects of vitamin E. Two recent well-conducted RCTs examined estrogen therapy for women with mild to moderate dementia and found no evidence of clinical benefit (49, 50).

### Pharmacologic Treatment for Vascular Dementia

The category of vascular dementia is heterogeneous, and the natural history of the disorder is not well understood (112). Some persons who meet criteria for vascular dementia exhibit a progressive functional decline similar to that seen in Alzheimer disease. Although antihypertensive treatment reduces the development of stroke and dementia, the evidence is limited that a similar course of treatment for persons with mild to moderate vascular dementia delays progression of the disease (51). One systematic review found that aspirin had no effect on cognitive symptoms in persons with vascular dementia (52). One RCT found that nimodipine (a calcium-channel blocker) had no effect on the cognitive and global symptoms of patients with vascular dementia (51), and 1 RCT found that galantamine at least stabilized CIBIC score and delayed cognitive deterioration among patients with vascular dementia as well as patients with Alzheimer disease and cerebrovascular disease (113).

### Neuroleptics

Even persons with mild dementia have a high prevalence of neuropsychiatric symptoms (114). A potential benefit of early detection of dementia is that these associated problems could be recognized and treated earlier with drugs such as neuroleptics. Although RCTs have examined these agents in persons with more severe dementia, no study has examined them in patients with mild to moderate dementia detected by screening.

### Antidepressants

Many people with mild to moderate dementia are depressed (114). Two RCTs provide evidence that antidepressants are effective for depressive symptoms among community-dwelling elderly persons with mild to moderate Alzheimer disease. One RCT with a crossover design showed that 6 weeks of therapy with clomipramine (a tricyclic antidepressant) reduced depressive symptoms (34). In a recent study, Lyketsos and colleagues (38) found that sertraline effectively treated depression in persons with both Alzheimer disease and major depression.

Although research demonstrates a positive effect of antidepressants on depression, it is not clear that these drugs modify the progression of dementia. No high-quality trial has examined the effect of antidepressants on health outcomes such as cognition, functional status, health-related quality of life, or clinician global impression of change.

### How Effective Are Nonpharmacologic Interventions for Persons with Mild to Moderate Dementia and Their Caregivers?

Nonpharmacologic interventions for dementia include behavioral training, caregiver education, and supportive services. Nonpharmacologic interventions may be directed at patients or their caregivers. Numerous studies have targeted patients with severe dementia, but no study has involved persons with mild to moderate dementia. Caregiver interventions are complex and varied but usually include at least one of the following components: support groups, individual or family counseling, skills training, or education. Interventions targeted to caregivers are usually studied for benefit to patients as well to caregivers themselves.

One systematic review (53) and five well-conducted RCTs (54–58, 115) have examined interventions directed at caregivers of persons with mild to moderate dementia (Table 5). The systematic review found no significant dif-

### Table 5. Summary of Efficacy of Caregiver Interventions

<table>
<thead>
<tr>
<th>Study, Year (Reference)</th>
<th>Patients, n</th>
<th>Patient Outcomes†</th>
<th>Caregiver Outcomes‡</th>
<th>Time to Nursing Home Placement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hebert et al., 1994 (54)</td>
<td>45</td>
<td>Not significant</td>
<td>Not significant</td>
<td>Not significant</td>
</tr>
<tr>
<td>Hebert et al., 1995 (55)</td>
<td>206</td>
<td>Not tested</td>
<td>Not tested</td>
<td>Significant</td>
</tr>
<tr>
<td>Mittelman et al., 1996 (56)</td>
<td>96</td>
<td>Not tested</td>
<td>Not tested</td>
<td>Significant</td>
</tr>
<tr>
<td>Brodaty et al., 1997 (59)</td>
<td>36</td>
<td>Not significant</td>
<td>Significant</td>
<td>Not tested</td>
</tr>
<tr>
<td>McCurry et al., 1998 (57)</td>
<td>42</td>
<td>Not significant</td>
<td>Significant</td>
<td>Not tested</td>
</tr>
</tbody>
</table>

* Significance and nonsignificance were measured statistically.
† Cognitive, functional, and behavioral symptoms.
‡ Included caregiver burden, depressive symptoms, and reaction to patients’ behavioral problems in the trials by Hebert et al.; caregiver burden, depressive symptoms, sleep problems, and reaction to patients’ behavioral problems in the trial by McCurry et al.; and caregiver burden and depressive symptoms in the trial by Marriott et al.
ferences in caregiver burden between intervention and control groups and concluded that little or no evidence shows that interventions to support caregivers of persons with Alzheimer disease yield quantifiable benefit (53). One other RCT had similar findings (115). The other four studies involved multicomponent interventions, and all had some positive results. Two studies focused on caregiver outcomes and found modest benefits (57, 58). The other two studies found that intensive, comprehensive caregiver interventions enabled caregivers to maintain affected persons at home for a substantially longer period (between 11 and 19 months longer) than caregivers who did not receive the intervention (59, 116).

Thus, several types of interventions targeted to caregivers showed a positive impact on varied outcomes. Because of the heterogeneity of the interventions, however, it is difficult to determine their optimal components. All of the studies were conducted among patients who had clinically detected disease and required caregivers. The extent to which such interventions would be useful for family members of persons with milder degrees of dementia detected by screening is not clear.

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

Persons identified by screening as having early dementia may have the opportunity to discuss the nature of the syndrome; its prognosis; and future planning with 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 decision making; consent to participate in research; and contemplate issues such as motor vehicle driving, self-neglect, financial victimization, and housing relocation. Screening may also permit earlier and more effective treatment of coexisting 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 for depression and anxiety, the time and cost of screening, and possible labeling effects. Because at least 50% of patients with a positive result on a screening test will not meet criteria for dementia, any screening program must be linked to a source of diagnostic interviews. Although these interviews could be done by primary care physicians, relatively few nonspecialist physicians engage in such interviews as standard practice. After a positive screening result, patients and families may have to wait to obtain a referral for a diagnostic work-up, potentially increasing anxiety and worry.

Screening will also detect mild cognitive impairment, a newly recognized condition that increases the risk for dementia (117). No well-conducted RCT, however, provides information about an effective treatment for persons with this disorder. Labeling such persons with a disease could potentially cause unnecessary anxiety. Once a patient receives a diagnosis of dementia, he or she is unlikely to qualify for long-term care insurance or acceptance into a continuous-care retirement community. Despite these potential hardships, however, surveys of elderly patients and caregivers of patients with Alzheimer disease show that most persons want to be told of a dementia diagnosis (118, 119).

The potential harms of treatment apply primarily to drugs, both cholinesterase inhibitors and others. Common side effects of cholinesterase inhibitors are nausea, vomiting, weight loss, and diarrhea. In the trials of galantamine, the dropout rate attributable to adverse events was 2% to 15% higher in the drug group than in the placebo group. In the trials of rivastigmine and higher-dose donepezil, the adverse effect rates were 5% to 20% higher and about 8% higher, respectively, in patients receiving the drugs. Tacrine has significant gastrointestinal and hepatic side effects, and the odds ratio for adverse event–related dropout among persons who took this drug was 5.7 (95% CI, 4.1 to 7.9). However, in general, fewer than 20% of patients stop taking cholinesterase inhibitors because of side effects. In RCTs of other drugs, dropout rates did not differ significantly between persons who took *Ginkgo biloba*, selegiline, 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 persons older than 85 years of age. Patients experience progressive cognitive and functional dependence, psychotic and depressive symptoms, and injuries. The burden of disease also extends to caregivers, who have high rates of emotional and financial stress and depression. Among all primary care patients older than 65 years of age who have dementia, approximately 50% have not received a diagnosis.

No randomized trial has evaluated the efficacy of dementia screening in primary care. The MMSE is the best-studied brief screening tool for dementia, but it has limited specificity when the cut-point is set for higher sensitivity, and scores must be adjusted for age and educational attainment. Other patient-based cognitive screening tests have similar characteristics. Although many of these tests take 10 minutes or less to administer, a screening program would require additional time for diagnostic interviews and patient and family counseling.

The most important problem with the evidence for screening for dementia is the uncertainty about the effectiveness of treatment for persons whose disease would be detected by screening. Cholinesterase inhibitor treatment...
of clinically detected mild to moderate Alzheimer disease has minimal impact on functional status but a modest and consistent tendency in some persons to stabilize cognition and clinician global impression of change. The literature makes it difficult to define clearly how many persons with early dementia benefit from this treatment, and by how much. The degree to which this evidence can be extrapolated to persons with dementia detected by screening is uncertain. Other pharmacologic treatments have not been adequately studied.

Limited evidence indicates that intensive multicomponent interventions to support caregivers may delay nursing home placement for persons with Alzheimer disease. However, such interventions have demonstrated few direct benefits for patients or caregivers. The relevance of this finding for the families of persons with screening-detected dementia, who presumably do not yet have caregivers, is unclear. Additional benefits of screening, including individual and family planning and better decisions about health care interventions for other conditions, have not been studied.

Important gaps remain in our knowledge about screening for and early treatment of dementia. An RCT of screening for dementia in primary care that prospectively evaluates many health outcomes would provide the best evidence of benefits and harms. A trial of screening is justifiable, given the high prevalence of undiagnosed dementia among primary care patients older than 65 years of age and the efficacy of cholinesterase inhibitor treatment for clinically detected mild to moderate Alzheimer disease. 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 use of health care, problem behaviors, psychiatric symptoms, and accidental injury are common in early dementia, little research to date has dealt with treatments to address these important aspects of the syndrome. The value of nonpharmacologic as well as pharmacologic interventions in patients with early dementia merits further study. Outcome measures should be reported to clarify how many persons benefit from these interventions, and by how much. Because dementia is progressive, outcome measures that incorporate time, such as time to decline or survival analyses, are most appropriate.

Although many uncertainties remain, the concept of detecting dementia at an early stage to allow interventions is a good one. Interventions are the only means by which to modify the otherwise certain decline of persons with this disorder. Screening for dementia is worth pursuing with further research.

From Indiana University School of Medicine, Indianapolis, Indiana; University of New Mexico School of Medicine, Albuquerque, New Mexico; and University of North Carolina School of Medicine, Chapel Hill, and RTI International, Research Triangle Park, North Carolina.

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Current author addresses, the Appendix Figures, and the Appendix Tables are available at www.annals.org.

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**CLINICAL GUIDELINES**

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Screening for Dementia in Primary Care

Clinical Guidelines


APPENDIX: METHODS

The RTI–University of North Carolina Evidence-based Practice Center, together with members of the USPSTF, sought to clarify issues concerning screening for dementia by performing a systematic review of the relevant scientific literature on this topic.

Analytic Framework

The systematic evidence review examined the evidence for screening for dementia. This summary of the evidence uses the information from the systematic evidence review, including the analytic framework. Appendix Figure 1 presents the analytic framework that we used to guide our literature search. The analytic framework describes the logical chain that must be supported by evidence to link screening to improved health outcomes. Each arrow in the analytic framework represents a key question (Appendix Table 1), and we searched systematically for evidence concerning each key question in the analytic framework.

The analytic framework begins on the left side of the figure with a primary care population at risk for dementia and moves to the right. The first key question (represented by the overarching arrow) examines direct evidence that screening improves health outcomes. The health outcomes of interest are improved function (including cognitive, social, and physical); reduced hospitalizations, institutionalizations, and health care visits; fewer behavioral problems; reduced caregiver stress; fewer injuries; and improved health-related quality of life. Since we found no such overview studies, we continued to examine the indirect evidence in the following key questions, represented as linkages in the analytic framework.

Key questions 2 and 3 examine the yield of screening, involving both the prevalence of undiagnosed dementia in the population and the accuracy and reliability of various screening tests. Farther to the right in the analytic framework, key question 4 examines the efficacy of various pharmacologic treatments, including treatment with antihypertensives or aspirin to prevent the progression of vascular dementia; treatment of persons with Alzheimer disease with cholinesterase inhibitors; and treatment of people with Alzheimer disease with other drugs, neuroleptics, or antidepressants. Key question 5 examines the effectiveness of nonpharmacologic interventions for patients or caregivers, and key question 6 involves the effect of knowledge about the diagnosis of dementia on family and individual planning.

The critical issue is the efficacy of these treatments among persons whose disease would be detected by screening. Many studies examine treatment for persons with clinically detected dementia; these are useful only insofar as they allow extrapolation to the efficacy of treatment at detection by screening. Furthermore, arrows 4 through 6 (and key questions 4 through 6) actually imply that the issue of interest is the added efficacy of initiating treatment after screening detection as opposed to initiation after clinical detection.

At the far right in the analytic framework are the health outcomes. In the end, the indirect evidence must allow a reasonable estimation of the magnitude of benefit in these outcomes that is attributable to screening. At the bottom of the analytic framework are linkage and key question 7, concerning harms of screening (for example, labeling), and key question 8, concerning harms of treatment (for example, side effects).

Eligibility Criteria for Admissible Evidence

The staff of the Evidence-based Practice Center and USPSTF liaisons developed eligibility criteria for selecting relevant evidence to answer the key questions (Appendix Table 2). For key question 1, we required a well-conducted RCT of screening of adequate size and length to estimate health outcomes with reasonable accuracy. For key questions 2 and 3, we required cross-sectional or cohort studies in which screening tests were performed in a primary care or general unselected population and were compared with an acceptable reference standard. For key questions 4 through 6, we accepted RCTs of treatments with health outcomes that provided information about the severity of dementia. For key questions 7 and 8, we required RCTs of screened (or treated) versus nonscreened (or nontreated) groups.

Literature Search Strategy, Results, and Review of Abstracts and Articles

The analytic framework and key questions guided our literature searches. We examined the critical literature described in the previous USPSTF review of this topic (published in 1996) (28) and used our eligibility criteria to develop search terms. We used the search terms to search MEDLINE and the Cochrane Library for English-language articles that met our inclusion criteria and were published between 1 January 1994 and 1 September 2002. We also examined the bibliographies of pertinent articles and contacted experts to obtain other references. When we found that a key question could best be answered by older literature, we also examined these studies. When we found that a systematic review used acceptable methods and that its studies met our criteria, we used the review instead of the individual studies. The search strategy and results are shown in Appendix Table 2 and Appendix Figures 1 through 8. All searches started with the term dementia and then proceeded by adding other terms as appropriate.

The first author and at least one other coauthor reviewed all abstracts found through our searches to determine which met our eligibility criteria. When either reviewer thought that an abstract might meet criteria, the article was copied for full review. The first author and at least one other coauthor reviewed each full article. Those that met eligibility criteria after full review (and discussion, when necessary) were abstracted. We critically appraised each study using criteria developed by the USPSTF (31). If we found a study or systematic review that met criteria but contained a methodologic flaw that invalidated its findings, we excluded it from further review. Abstracted articles or systematic reviews that met eligibility criteria and had no fatal flaws were entered into predesigned evidence tables (see Appendix B in the systematic evidence review “Screening for the Dementia Syndrome,” available at www.preventiveservices.ahrq.gov).

Development of the Systematic Evidence Review and Summary of the Evidence Article

The authors presented an initial work plan, including a provisional analytic framework and key questions, to the entire Task
Appendix Table 1. Key Questions for Screening for Dementia Syndrome

<table>
<thead>
<tr>
<th>Question</th>
<th>Evidence Needed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Is there direct evidence from a randomized, controlled trial of screening that screening for dementia improves health outcomes?</td>
<td></td>
</tr>
<tr>
<td>2. How common is undiagnosed dementia?</td>
<td></td>
</tr>
<tr>
<td>3. How accurate are the screening tests?</td>
<td></td>
</tr>
<tr>
<td>4. What is the added efficacy of initiating the pharmacologic treatments below at screening detection compared with clinical detection in improving health outcomes?</td>
<td>Antihypertensives and aspirin for vascular dementia</td>
</tr>
<tr>
<td></td>
<td>Cholinesterase inhibitors for Alzheimer disease</td>
</tr>
<tr>
<td></td>
<td>Other drugs (e.g., Ginkgo biloba, selegiline, vitamin E, estrogen) for Alzheimer disease</td>
</tr>
<tr>
<td></td>
<td>Neuroleptics</td>
</tr>
<tr>
<td></td>
<td>Antidepressants</td>
</tr>
<tr>
<td>5. What is the efficacy of nonpharmacologic interventions for persons with mild to moderate dementia and their caregivers?</td>
<td></td>
</tr>
<tr>
<td>6. Does earlier knowledge of the diagnosis of dementia improve patient and family planning for future care and safety?</td>
<td></td>
</tr>
<tr>
<td>7. What are the harms of screening?</td>
<td></td>
</tr>
<tr>
<td>8. What are the harms of treatment?</td>
<td></td>
</tr>
</tbody>
</table>

Appendix Table 1. Key Questions for Screening for Dementia Syndrome

A draft systematic evidence review was presented to the Task Force and then sent for broad peer review. The peer review involved individual experts in the field, representatives of relevant professional organizations, and representatives of appropriate federal agencies. We revised the evidence review as appropriate after receiving peer review comments. The Task Force reviewed all information and voted on a recommendation. We then put the systematic evidence review into final form and from it developed the manuscript for journal publication.

Current Author Addresses: Dr. Boustani: Regenstrief Institute, Inc., 1050 Wishard Boulevard, RG 6, Indianapolis, IN 46202-2872.
Dr. Peterson: University of North Carolina at Chapel Hill, 706C Hibbard Drive, Chapel Hill, NC 27514.
Dr. Hanson: University of North Carolina at Chapel Hill, 258 Mack尼der, CB #7110, Chapel Hill, NC 27599.
Dr. Harris: Sheps Center for Health Services Research, 725 Airport Road, CB #7590, Chapel Hill, NC 27599-2949.
Dr. Lohr: RTI International, 3040 Cornwallis Road, Research Triangle Park, NC 27709.
## Appendix Table 2. Dementia Syndrome: Eligibility Criteria, Search Strategy, and Results of Searches*

<table>
<thead>
<tr>
<th>Key Question</th>
<th>Inclusion Criteria</th>
<th>Systematic Reviews Found</th>
<th>Full Articles Reviewed</th>
<th>Systematic Reviews and Articles That Met Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>Dementia syndrome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Published 1 January 1994–1 September 2002</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>English language</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Human subjects age ≥60 y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cochrane Library, MEDLINE, PsycINFO, EMBASE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Direct evidence of screening</td>
<td>RCTs Mass screening</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2. Prevalence of undiagnosed dementia</td>
<td>Systematic reviews Cross-sectional prevalence Age ≥60 y in community or outpatient setting Blinded, independent evaluation for dementia syndrome diagnosed by DSM-III, DSM-III-R, or DSM-IV Exclusion of patients with previous diagnosis of dementia syndrome Valid assessment of lack of previous diagnosis</td>
<td>0</td>
<td>MEDLINE: 6 PsycINFO: 1 Total: 7</td>
<td>Systematic reviews: 0 Additional studies: 4 Total: 4</td>
</tr>
<tr>
<td>3. Accuracy of screening tests</td>
<td>Systematic reviews Age ≥60 y in community or outpatient setting Blinded, independent evaluation for dementia syndrome diagnosed by DSM-III, DSM-III-R, or DSM-IV Exclusion of patients with previous diagnosis of dementia syndrome Data provided for true-positive, true-negative, false-positive, and false-negative results</td>
<td>Cochrane Library: 1 PsycINFO: 1 Other: 1 Total: 3</td>
<td>MEDLINE: 44 PsycINFO: 21 Other: 10 Total: 75</td>
<td>Systematic reviews: 1 Additional studies: 9 Total: 10</td>
</tr>
<tr>
<td>4. Efficacy of pharmacologic treatment</td>
<td>Systematic reviews RCTs Age ≥60 y in community or outpatient setting Reference standard for all patients Intervention one of defined key questions Any of the 6 outcomes from the analytic framework</td>
<td>Cochrane Library: 12 MEDLINE: 21 EMBASE: 3 Total: 36</td>
<td>Cochrane Library: 0 MEDLINE: 232 PsycINFO: 7 EMBASE: 27 Other: 33 Total: 299</td>
<td>Reviews: 12 RCTs: 19 Total: 31</td>
</tr>
<tr>
<td>5. Efficacy of nonpharmacologic treatment</td>
<td>Systematic reviews RCTs Age ≥60 y in community or outpatient setting Reference standard for all patients Intervention directed at patients or caregivers Health outcomes</td>
<td>Cochrane Library: 0 MEDLINE: 1 EMBASE: 0 Total: 1</td>
<td>Cochrane Library: 0 MEDLINE: 6 PsycINFO: 0 EMBASE: 0 Total: 6</td>
<td>Reviews: 1 RCTs: 6 Total: 7</td>
</tr>
<tr>
<td>6. Efficacy of interventions for planning</td>
<td>Systematic reviews RCTs Age ≥60 y in community or outpatient setting Reference standard for all patients Improved planning for future care</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>7. Harms of screening</td>
<td>Systematic reviews RCTs Age ≥60 y in community or outpatient setting Reference standard for all patients Any treatment Any possible harms of screening</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>8. Harms of treatment</td>
<td>Systematic reviews RCTs Age ≥60 y in community or outpatient setting Reference standard for all patients Any treatment Any possible harms of treatment</td>
<td>Cochrane Library: 12 MEDLINE: 9 EMBASE: 2 Total: 23</td>
<td>Cochrane Library: 0 MEDLINE: 228 EMBASE: 20 PsycINFO: 7 Other: 2 Total: 257</td>
<td>Reviews: 9 RCTs: 10 Total: 19</td>
</tr>
</tbody>
</table>

* DSM-III = Diagnostic and Statistical Manual of Mental Disorders, third edition; DSM-III-R = Diagnostic and Statistical Manual of Mental Disorders, third edition, revised; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, fourth edition; RCT = randomized, controlled trial.
Appendix Figure 1. Analytic framework for screening for dementia.

KQ = key question.

Appendix Figure 2. Selection of articles for key question 1: direct evidence.

RCT = randomized, controlled trial.

Appendix Figure 3. Selecting articles for key question 2: prevalence of undiagnosed dementia.
Appendix Figure 4. Selecting articles for key question 3: accuracy of screening tests.

Appendix Figure 5. Selecting articles for key question 4: efficacy of pharmacologic treatment.

Appendix Figure 6. Selecting articles for key question 5: efficacy of nonpharmacologic treatment.

Appendix Figure 7. Selecting articles for key question 6: interventions for planning.

Appendix Figure 8. Selecting articles for key questions 7 and 8: harms of screening and treatment.

RCT = randomized, controlled trial.