

# Screening for Dementia: Recommendations and Rationale: United States Preventive Services Task Force

United States Preventive Services Task Force

## Citation

United States Preventive Services Task Force. *Screening for Dementia: Recommendations and Rationale: United States Preventive Services Task Force*. The Internet Journal of Mental Health. 2003 Volume 2 Number 1.

## Abstract

### Figure 3



Agency for Healthcare Research and Quality

### Figure 2



US Department of Health and Human Services

## SUMMARY OF RECOMMENDATION

The U.S. Preventive Services Task Force (USPSTF) concludes that the evidence is insufficient to recommend for

or against routine screening for dementia in older adults. I recommendation.

The USPSTF found good evidence that some screening tests have good sensitivity but only fair specificity in detecting cognitive impairment and dementia. There is fair to good evidence that several drug therapies have a beneficial effect on cognitive function (equivalent to delaying the natural progression of Alzheimer's disease from 2 to 7 months), but the evidence of their beneficial effects on instrumental activities of daily living is mixed, with the benefit being small, at best. There is insufficient evidence to determine whether the benefits observed in drug trials are generalizable to patients whose disease would be detected by screening in primary care settings. The accuracy of diagnosis, the feasibility of screening and treatment in routine clinical practice, and the potential harms of screening (eg, labeling effects) are also unknown. The Task Force therefore could not determine whether the benefits of screening for dementia outweigh the harms.

## CLINICAL CONSIDERATIONS

- The Mini-Mental Status Examination (MMSE) is the best-studied instrument for screening for cognitive impairment. When the MMSE is used to screen unselected patients, the predictive value of a positive result is only fair. The accuracy of the MMSE depends upon a person's age and educational level: using an arbitrary cut-point may potentially lead to more false-positives among older people with lower educational levels, and more false-negatives among younger people with higher educational levels. Tests that assess functional limitations rather than cognitive impairment, such as the Functional Activities Questionnaire (FAQ), can detect dementia with

sensitivity and specificity comparable to that of the MMSE.

- Early recognition of cognitive impairment, in addition to helping make diagnostic and treatment decisions, allows clinicians to anticipate problems the patients may have in understanding and adhering to recommended therapy. This information may also be useful to the patient's caregiver(s) and family member(s) in helping to anticipate and plan for future problems that may develop as a result of progression of cognitive impairment.
- Although current evidence does not support routine screening of patients in whom cognitive impairment is not otherwise suspected, clinicians should assess cognitive function whenever cognitive impairment or deterioration is suspected, based on direct observation, patient report, or concerns raised by family members, friends, or caretakers.

## **SCIENTIFIC EVIDENCE**

### **EPIDEMIOLOGY AND CLINICAL CONSEQUENCES**

Dementia is defined as 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.<sup>4</sup> The USPSTF did not review evidence on screening individuals with “mild cognitive impairment,” a condition not associated with functional impairment but that sometimes progresses to dementia.<sup>5</sup>

Alzheimer's disease and cerebrovascular ischemia (vascular dementia) are the two most common causes of dementia. Between 60% and 70% of individuals with dementia have Alzheimer's disease; about 20% to 30% have either vascular dementia or a combination of vascular dementia and Alzheimer's disease.<sup>3</sup> Dementia causes a high burden of suffering for patients and their families. For patients, it increases dependency and complicates other medical conditions. For families it can lead to anxiety and depression, and may increase the time needed to care for loved ones. The annual economic cost of dementia is estimated to be \$100 billion.<sup>6</sup>

Age is the strongest risk factor for dementia: 3% to 11% of

people older than 65, and 25% to 47% of those older than 85 have dementia.<sup>2</sup> First degree relatives of patients with Alzheimer's disease have a cumulative lifetime risk of 39%, approximately twice the risk of Alzheimer's disease in the general population.<sup>7</sup> Some genetic mutations have been associated with Alzheimer's disease: about 20% to 30% of the general population and 45% to 60% of people with late-onset Alzheimer's disease have the apolipoprotein E-4 (APOE-4) gene.<sup>8</sup> Cardiovascular risk factors such as hypertension are associated with an increased risk of both Alzheimer's disease and vascular dementia.<sup>9,10,11</sup>

### **ACCURACY AND RELIABILITY OF SCREENING TESTS**

Screening tests used for dementia are either direct cognitive tests of patients or functional assessments using patients and others as informants. Most screening tests have been evaluated in studies with small sample sizes, and the populations of patients on whom screening instruments have been tested have varied greatly, making it difficult to determine the overall performance of screening tests for dementia. The best evidence is available for a cognitive test – the Mini-Mental Status Examination (MMSE) – from studies in primary care settings that used standardized diagnostic instruments (eg, the DSM-IV) as a “gold standard.” Depending upon the cutpoint used for an abnormal test, the sensitivity of MMSE for dementia ranges from 71% to 92%, and the specificity ranges from 56% to 96%.<sup>12,13,14,15,16,17,18,19</sup> The predictive value of a positive test, in a population with 10% prevalence of dementia, may range from 15% to 72%.<sup>2</sup> A drawback of MMSE is that its accuracy depends upon age, education, and ethnicity of the individual; it is most accurate for whites with at least a high school education.<sup>2</sup> Other cognitive screening tests, such as the Short Portable Mental Status Questionnaire, Clock Drawing Test, Modified MMSE, Mini-Cog, Hopkins Verbal Learning Test, and the 7-minute screen are promising, but have not been adequately evaluated in primary care settings.<sup>2</sup>

Some informant-based functional tests, such as the Functional Activities Questionnaire (FAQ), the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE), and the Instrumental Activities of Daily Living (IADL) Questionnaire, have also been tested.<sup>3,12,17</sup> The sensitivity and specificity of FAQ is reported to be 90%.<sup>12</sup> The functional test instruments offer the advantages of “everyday relevance,” acceptability by subjects, adaptability to various types of patients, administrative ease, longitudinal

perspective, and cross-cultural portability. The primary limitations of these tests are that not all patients have caregivers and that some functions (eg, cognition) are not tested. Most importantly, few methodologically sound studies regarding the accuracy of these questionnaires in primary care settings have been completed.

Testing for genetic mutations may eventually prove useful in screening individuals at risk for Alzheimer's disease. There are, however, limited population-based data regarding the absolute risk of dementia among individuals having a positive genetic test. Thus the potential benefits and harms of testing for an individual patient are uncertain. Finally, the ethical issues in genetic testing for dementia are unresolved.

### **EFFECTIVENESS OF EARLY DETECTION**

The USPSTF found no direct evidence examining the effectiveness of screening for dementia in primary care settings in which the clinical outcomes of a population of patients who are screened, diagnosed, and treated are compared with outcomes in a population receiving usual care. To assess possible benefits of detecting undiagnosed dementia, the USPSTF examined trials of therapies aimed at improving the cognitive function of patients with dementia. The natural history of Alzheimer's disease is of progressive decline in cognitive function, thus an "improvement" from an intervention means a slowing of the rate of decline.

### **PHARMACOLOGICAL INTERVENTIONS**

**Cholinesterase inhibitors:** The best evidence is available for cholinesterase inhibitors, which have been studied in randomized control trials (RCTs) lasting 6-12 months in patients with mild to moderate Alzheimer's disease. There are 2 scales of function commonly used in research on dementia: a 70-point Alzheimer's Disease Assessment Scale for Cognition (ADAS-Cog) and a 7-point Clinician's Interview Based Impression of Change plus caregiver input scale (CIBIC). Four systematic reviews<sup>20,21,22,23</sup> and 5 RCTs<sup>24,25,26,27,28</sup> have examined the effect of cholinesterase inhibitors compared with placebo among people with mild to moderate Alzheimer's disease. Most of these studies found a statistically significant difference favoring cholinesterase inhibitors that ranged from 2.1 to 3.4 points on ADAS-Cog. A slowing of decline by 2 to 3 ADAS-Cog points over a year is approximately equivalent to a delay in disease progression of up to 7 months in a person with mild dementia, or a delay of 2 to 5 months in a person with moderate dementia.<sup>2</sup> In addition, several of these studies showed that cholinesterase inhibitors stabilized or slightly improved clinician

impression of change as measured by CIBIC. However, the evidence of the effects of cholinesterase inhibitors on functional measures, such as instrumental activities of daily living, is mixed. In general, the studies have shown little or no effect of cholinesterase inhibitors on functional decline after 6 months of treatment, and a small, but statistically significant, difference from placebo after 12 months of treatment.<sup>29,30,31,32,33</sup>

**Ginkgo biloba, selegiline, vitamin E, and estrogen:** The evidence is weak that other drugs besides cholinesterase inhibitors have important benefits in Alzheimer's disease. A meta-analysis that examined only the 4 highest quality RCTs found a small (approximately 3%) difference in cognitive scales between patients taking ginkgo biloba compared with placebo.<sup>34</sup> A recent Cochrane review and meta-analysis of 15 placebo-controlled studies found that using selegiline led to no clinically important differences from placebo.<sup>35</sup> A well-conducted 2-year RCT of the effect of vitamin E on moderate Alzheimer's disease found no effect on cognition and limited evidence that it delayed institutionalization.<sup>36</sup> A well-conducted RCT examined estrogen therapy for women with mild to moderate dementia and found no evidence of clinical benefit.<sup>37</sup>

**Pharmacotherapy for vascular dementia:** Although antihypertensive treatment reduces the development of stroke and dementia, the evidence is limited that similar treatment of people with mild to moderate dementia delays disease progression.<sup>38</sup> Recent studies have found no clinical benefit of nimodipine or aspirin in people with vascular dementia.<sup>38,39</sup>

### **NON-PHARMACOLOGICAL INTERVENTIONS**

Several studies have examined non-pharmacological interventions (eg, behavioral training, caregiver education, and supportive services), directed either at the patient or the caregiver, in improving patient or caregiver outcomes. A systematic review and a RCT examined interventions directed at caregivers of people with mild to moderate dementia and found no significant differences in caregiver burden between intervention and control groups.<sup>40,41</sup> Four well-conducted RCTs testing multi-component interventions yielded positive benefits. Two produced modest benefits in caregiver outcomes,<sup>42,43</sup> and 2 studies found that intensive, comprehensive caregiver interventions enabled the caregivers to maintain affected persons at home for a 11 to 19 months longer compared with those who did not receive the intervention.<sup>44,45</sup> None of these studies demonstrated a

significant impact on patient outcomes. Subjects in these studies had clinically diagnosed disease and needed caregivers. The extent to which such interventions would be useful to caregivers of people with milder degrees of dementia (as is likely to occur in those detected by screening) is unclear. Additionally, these studies used multi-component interventions, making it difficult to assess the impact of individual components. These factors make it difficult to generalize the potential benefits of these interventions to patients who would be detected by routine screening in primary care settings.

Early detection and treatment of dementia due to a reversible cause is a potential benefit of screening for dementia. The USPSTF reviewed evidence to assess the prevalence of dementias due to conditions such as vitamin B12 deficiency, thyroid disease, neurosyphilis, normal pressure hydrocephalus, or sleep apnea. No study provided information applicable to a screened population; the data from studies done in specialty clinics indicate that only 1.5% of cases could be classified as fully reversible dementia.<sup>3</sup>

## **POTENTIAL ADVERSE EFFECTS OF SCREENING**

The harms of dementia screening have not been systematically examined. Both false-positive and true positive results could have adverse psychological effects on patients, but the USPSTF found few studies that address these outcomes. In one study of patients undergoing a detailed assessment of mental function, fewer than 5% found the screening itself distressing, intrusive or depressing<sup>46</sup>; no studies were found of patient attitudes towards more limited tests of cognitive function such as the MMSE. Once screening identifies an individual with low cognitive function, clinicians have some concern over the disclosure of information to patients regarding their dementia status. The USPSTF found several case reports of suicide in patients with newly diagnosed Alzheimer's disease,<sup>47,48</sup> but found no evidence of this potential adverse event in screening studies. A diagnosis of dementia could have effects on a patient's autonomy, but the USPSTF found no evidence supporting this concern. More established risks of receiving the diagnosis of dementia are difficulty obtaining medical or life insurance, or acceptance into assisted-living communities.

The most commonly reported adverse effects in patients taking cholinesterase inhibitors are nausea, vomiting, weight loss, and diarrhea. Tacrine also has significant gastrointestinal and hepatic adverse effects. The dropout

rates in RCTs of cholinesterase inhibitors were higher in the groups taking cholinesterase inhibitors than in those taking placebo. In RCTs of other drugs, dropout rates did not differ significantly between those who took ginkgo biloba, selegiline, or vitamin E and those who took placebos.

## **RECOMMENDATIONS OF OTHERS**

There are no formal recommendations for routine screening for dementia. The American Academy of Neurology and the Canadian Task Force on Preventive Health Care concluded that there is insufficient evidence to recommend cognitive screening of asymptomatic individuals.<sup>49,50</sup> The American Medical Association and the American Academy of Family Physicians recommend that physicians be alert for cognitive and functional decline in elderly patients for recognition of dementia in its early stages.<sup>51,52</sup>

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The USPSTF recommendations are independent of the U.S. government. They do not represent the views of the Agency for Healthcare Research and Quality (AHRQ), the U.S. Department of Health and Human Services, or the U.S. Public Health Service.

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## **APPENDIX A**

### **U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS AND RATINGS**

The Task Force grades its recommendations according to one of 5 classifications (A, B, C, D, I) reflecting the strength of evidence and magnitude of net benefit (benefits minus harms):

A. The USPSTF strongly recommends that clinicians routinely provide [the service] to eligible patients. The USPSTF found good evidence that [the service] improves important health outcomes and concludes that benefits substantially outweigh harms.

B. The USPSTF recommends that clinicians routinely provide [this service] to eligible patients. The USPSTF found at least fair evidence that [the service] improves important health outcomes and concludes that benefits outweigh harms.

C. The USPSTF makes no recommendation for or against

routine provision of [the service]. The USPSTF found at least fair evidence that [the service] can improve health outcomes but concludes that the balance of benefits and harms is too close to justify a general recommendation.

D. The USPSTF recommends against routinely providing [the service] to asymptomatic patients. The USPSTF found at least fair evidence that [the service] is ineffective or that harms outweigh benefits.

I. The USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing [the service]. Evidence that [the service] is effective is lacking, of poor quality, or conflicting and the balance of benefits and harms cannot be determined.

## **APPENDIX B**

### **U.S. PREVENTIVE SERVICES TASK FORCE STRENGTH OF OVERALL EVIDENCE**

The USPSTF grades the quality of the overall evidence for a service on a 3-point scale (good, fair, poor):

Good: Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes.

Fair: Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies, generalizability to routine practice, or indirect nature of the evidence on health outcomes.

Poor: Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

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