Alzheimer’s disease (AD) is the primary cause of dementia in individuals over age 65, affecting more than 4 million individuals in the United States and more than 16 million individuals worldwide. Increasing age is the greatest risk factor for AD, and the U.S. population is aging rapidly; as such, by 2040 the number of individuals with Alzheimer’s disease is expected to increase to 14 million in the United States alone. The incidence of dementia doubles approximately every 5 years in individuals between the ages of 65 and 95 and by some estimates may reach nearly 50% by age 85.1 The fourth leading cause of death in the United States—after heart disease, cancer, and stroke—AD accounts for nearly 100,000 deaths annually and carries an annual cost of $110 billion.

Yet, despite the increasing prevalence of AD, the enormous emotional and financial costs, and the emerging treatments for the disease, AD continues to be underdiagnosed. By some estimates, fewer than one-half of all AD patients are currently diagnosed,2-5 and approximately 25% are treated with antidementia compounds.6 Routine screening is one strategy that has been proposed to help combat underdiagnosis of AD. There has been a rapid proliferation in both screening initiatives and instruments over the past 10 years. Various organizations have advocated community screening (table 1).7 The goal is to make screening for cognitive impairment as routine as screening for hypertension, hypercholesterolemia, prostate, or breast cancer. Although this approach appears obvious, it is not without its critics and has met with resistance due to pragmatic and theoretical issues.

In this article, we will briefly review the arguments for and against screening and suggest several strategies and instruments that may be helpful in the context of screening for Alzheimer’s disease in primary care practice.

**To screen**

Underdiagnosis of AD. Alzheimer’s disease is particularly underdiagnosed in primary care settings, perhaps because patients with early AD may appear entirely appropriate in the context of a
Table 2 provides a list of barriers to early detection. By some estimates, up to 95% of cases of mild dementia are not detected by clinicians. In one small study, 78.6% of patients with mild dementia, 71.4% with moderate dementia, and 20% with severe dementia had no indication of cognitive deficits in their medical records. Other studies in primary care practices have found rates of dementia between 50% and 66%.

**Benefits of medication.** There are four FDA-approved medications for the treatment of Alzheimer’s disease (donepezil, galantamine, rivastigmine, memantine). Each of these medications provides “symptomatic benefit” (ie, facilitates function of remaining neurons/synapses), but does not protect against subsequent neuronal loss (ie, no “disease-modifying” properties). The cholinesterase inhibitors (donepezil, galantamine, rivastigmine) are approved for mild-to-moderate AD, and data suggests they are most beneficial when administered early in the course of disease. Memantine is approved for moderate-to-late stage AD.

The emergence of potentially disease-modifying treatments further emphasizes the need for early detection and diagnosis. Drugs in current clinical trials are being evaluated for their ability to alter amyloid production or aggregation, and others that may clear brain amyloid. Early detection and treatment will be the key to the eventual success of disease-modifying drugs.

**Implementation of social support systems.** Implementation of social support systems to address issues of care, nutrition, and safety, as well as financial and legal planning, are most beneficial when initiated early in the course of a progressive disease. For example, patients with AD have increased risk for automobile accidents and do not accurately report symptoms of comorbid illnesses. Early screening and diagnosis of AD would allow patients and families to make decisions regarding transportation, living arrangements, and other aspects of care when the patient is functioning at the highest possible level.

**Not to screen**

The U.S. Preventive Services Task Force (USPSTF) position. The USPSTF evaluated screening for AD in 1996 and 2003. As in the 1996 report, the 2003 report did not endorse routine screening for AD. Although the report raised a number of concerns regarding screening for AD, including a low prevalence of AD, insufficient evidence for the accuracy of screening tests, low accuracy of screen-
ing tests for mild dementia, and biases for age, education, and ethnicity, the primary rationale for not endorsing screening is that until studies demonstrate that screening (and by implication, earlier diagnosis) provides better outcomes for patients with AD, endorsement is premature. The USPSTF does, however, recognize the potential importance of screening and suggests that screening to detect dementia at an early stage is desirable because only early intervention can modify an otherwise certain decline. Rather than endorsing screening at present, however, it endorsed further research in screening for dementia.

The Alzheimer's Association position. In 2000, the National Alzheimer’s Association formed the Work Group on Screening for Cognitive Impairment and Alzheimer’s Disease in an effort to develop guidance for its chapters. The 2000 work group listed 21 questions that should be considered before embarking on a public screening program, but it did not endorse community-based screening for AD. In the Alzheimer’s Association’s 2005 guidelines to the local chapters, the Association recognizes the potential benefits of early detection of AD, but again raises concerns, including the possible need for informed consent, the challenges of providing adequate follow-up in the case of a positive screen, variability in professional training and ability of those carrying out screening, and it reiterates the concerns of the USPSTF.

The Alzheimer’s Association position further distinguishes three levels of screening that are currently being used in community settings:

- **Level I** Memory awareness or pre-screening for memory problems
- **Level II** Community assessment of memory problems (using the MMSE and other such tests administered in a variety of settings)
- **Level III** Comprehensive diagnostic work-up (by a physician).

The association states “there seems to be no major problems with Levels I and III.” It does not, however, endorse Level II. In conclusion, the Alzheimer’s Association recommended against community screening by its chapters.

The Alzheimer’s Association does not explicitly comment on widespread screening by PCPs, either in the office or in collaboration with community-based groups. The Association does recommend public awareness programs based on “The 10 Warning Signs of Alzheimer’s Disease” as an alternative to most memory screening activities. Notably, these warning signs have not been validated and are not being promoted as a screening instrument. Nevertheless, this list bears a resemblance to recently developed informant questionnaires that are now being used to screen, and that, significantly, have been validated. Of some concern is that individuals experiencing cognitive deficits and their families may treat the 10 warning signs as a screening instrument, raising exactly the same concerns the Alzheimer’s Association raises regarding community screening.

**Screening in primary care**

**Who should be screened.** The goal of any screening program is to identify the largest number of individuals who have a particular disease in the most efficient manner. Efficiency includes us-

### Table 1 Recent screening initiatives

- Legislation signed by President Bush to make memory screening more accessible.
- “Welcome to Medicare” physical examination, which some groups have suggested include a memory screen.
- Recent efforts by several major pharmaceutical companies to promote regional and national screening efforts.
- Alzheimer’s Association declaration of November 16th as National Alzheimer’s Screening Day.
- A pilot regional screening day conducted at 10 New England sites in 1999.

Source: Created for GERIATRICS by PR Solomon and CA Murphy.

### Table 2 Barriers to early detection of Alzheimer’s disease

- Patient is often unaware, denies, or minimizes symptoms.
- Evaluation may be time-consuming and not well compensated financially.
- Belief that memory loss and cognitive decline are part of normal aging.
- Belief by some healthcare professionals and the general public that AD is not treatable.

Source: Created for GERIATRICS by PR Solomon and CA Murphy.

### Table 3 Recommendations for screening for Alzheimer’s disease in primary care practice

<table>
<thead>
<tr>
<th>Age range</th>
<th>Prevalence</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>65-74</td>
<td>3%</td>
<td>Discretionary, based on risk factors including family history and cognitive complaints from either patients or family.</td>
</tr>
<tr>
<td>75-84</td>
<td>19%</td>
<td>Every 2 years or if there are cognitive complaints from either patients or family.</td>
</tr>
<tr>
<td>&gt;85</td>
<td>47%</td>
<td>Annually.</td>
</tr>
</tbody>
</table>

Source: Created for GERIATRICS by PR Solomon and CA Murphy based on information from reference 1.
ing instruments that are accurate and brief. One way to increase the efficiency of instruments is to screen individuals who are at risk. In AD, the greatest risk factor is age. As such, screening groups of older individuals will have a higher yield. Some practitioners who refer to our clinic now report that they routinely screen all patients over age 65 on an annual basis. The prevalence of AD in this age group is 10%; prevalence becomes 20% in the 75- to 84-year-old range; prevalence may be as high as 48% in those over age 85.1 Other strategies to “enrich” the screening population are to screen those with a family history, or those with cognitive complaints, either from them or from family members. Table 3 summarizes the prevalence for various age groups and proposes screening guidelines for each group.

Selecting a screening instrument. Over the past 10 years, there has been a proliferation of screening instruments for AD (table 5).18-27 Screening instruments for AD fall into two categories:

### Prevalence of Alzheimer’s Disease

**With age:**
- **Age >65:** 10%
- **Age 75-84:** 20%
- **Age >85:** 48%

- **Clinician-administered neuropsychological instruments**
- **Questionnaires that are completed by the patient and/or an informant.**
- **Clinician-administered instruments** vary in scope, but most contain questions regarding orientation to time and place, recent memory, language, and visuospatial function. They may also contain questions to evaluate attention and concentration, executive function, and semantic memory. Clinician-administered instruments far outnumber informant-based screens. Table 4 lists some of the criteria desirable for a clinician-administered instrument to be accurate and useful in the primary care setting. A screening instrument with high sensitivity and specificity, requiring minimal time to administer, and that can be administered and scored by a variety of people in the office with minimal training may be appropriate for the primary care setting.

### Informant-based questionnaires

Informant-completed questionnaires for AD consist of a series of questions that are completed by a knowledgeable informant, typically a spouse, child, or close friend. These questions may in-
quire about cognition, mood and behavior, and function. Informant-based instruments are becoming more prevalent. These instruments have a number of advantages over clinician-administered screens, including:

1. They require no time from medical professionals to administer and minimal time to score
2. They do not require the cooperation of the patient
3. They can potentially be completed via telephone, mail, or internet
4. They can be completed by the informant confidentially.

In practice, the use of both clinician-administered and informant-based screens may be best. In cases where the patient is not present or cooperative, or office time is limited, informant-based instruments will prevail. Obviously, when the patient comes unaccompanied, clinician-administered instruments are necessary. It may be possible to gain more accuracy by combining the two types of instruments. In the case of a negative informant-based screen, the clinician must also be wary of underreporting by the informant that can lead to a false negative.

**Table 5 Desirable characteristics for a clinician-administered screening instrument for Alzheimer’s disease**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>High sensitivity*</td>
<td>Low sensitivity leads to false negatives, meaning missed diagnoses and patients with disease left untreated.</td>
</tr>
<tr>
<td>High specificity+</td>
<td>Low specificity leads to false positives. False positives may lead to unnecessary, time-consuming, and expensive evaluations, and may cause unnecessary anxiety in patients and their families.</td>
</tr>
<tr>
<td>Short administration</td>
<td>Clinician and staff time in primary care practices is limited. Instruments that require longer periods of clinician/staff time are less likely to be used.</td>
</tr>
<tr>
<td>Training of the screen administrator</td>
<td>Instruments that require minimal training to administer and/or have clear instructions, including training videos, are more likely to be used.</td>
</tr>
<tr>
<td>Simplicity of rules for scoring</td>
<td>Some screening instruments are scored by clear rules that leave no room for clinical judgment. Other instruments have questions for which clinicians have difficulty agreeing on the scoring criteria (eg, spelling “world” backwards on the MMSE)</td>
</tr>
</tbody>
</table>

*Sensitivity is the percentage of individuals with the disease who screen positive.
+ Specificity is the percentage who do not have the disease who screen negative.

Source: Created for GERIATRICS by PR Solomon and CA Murphy.

Reassure the patient: A positive screen does not mean you have AD, but it does suggest further testing is required.

Positive screening results provide the physician an opportunity to discuss with the patient the need for further memory evaluations. The PCP might conduct this evaluation or refer it to a specialty memory clinic, neurologist, or psychiatrist. Much like a positive screen for breast or prostate cancer, the patient needs to be reassured that the positive screen does not mean that he/she has AD, but simply suggests that a more thorough evaluation is warranted.

Negative screening results provide the opportunity to reassure the patient that although they may be experiencing memory changes, these changes are consistent with the normal, healthy aging process and are not likely to be indicative of Alzheimer’s disease or other contribute to instrument selection. For example, the Mini-Mental State Examination (MMSE), the most widely used screening instrument, has a relatively low accuracy and is influenced by educational and socioeconomic levels.

**Administering the screening instrument.** Once the screening criteria are selected, one professional in the practice generally assumes responsibility for screening. The qualifications of the professional will depend upon the screening instrument used (table 4). For instruments requiring minimal clinical judgment to administer or score, RNs and sometimes trained office staff can administer the test; for more complex instruments NPs, PAs, and physicians may be required. If the instrument is clinician-based, the professional may administer and score the screen. If the instrument is informant-based, the professional needs to ensure that the informant fills out the instrument and that the instrument is scored BEFORE the patient sees the physician. Armed with the results of the screen prior to meeting with the patient, the physician has the opportunity to discuss the findings with the patient when they meet.

**Providing feedback to the patient/family.** The goal of screening is to identify AND diagnose individuals with a dementing illness.

In the case of a negative informant-based screen, the clinician must also be wary of underreporting by the informant that can lead to a false negative. In these cases a clinician-administered screen should follow.

Other factors, including the instrument’s accuracy (sensitivity and specificity) and the patient’s socioeconomic and educational level, will also contribute to instrument selection. For example, the Mini-Mental State Examination (MMSE), the most widely used screening instrument, has a relatively low accuracy and is influenced by educational and socioeconomic levels.

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dementing illness. As in the case of the positive screen, it is important to discuss with the patient that a negative screen does not guarantee that dementia is not present. On occasion, a family member, close friend, or even the patient, will note that despite a negative screen, they continue to be concerned. In these cases, it is our policy that the view of the individual takes precedence over the results of the screen, and we recommend a full evaluation.

**Conclusion**

There is an emerging consensus that the three keys to the eventual successful treatment of Alzheimer’s disease are:

1. Early detection
2. Using currently approved medications to provide symptomatic treatment
3. Developing treatments to slow and eventually halt disease progression.

If early detection of Alzheimer’s disease is the first step in successful treatment and management, screening would seem to be an important strategy.

**References**