



Perspectives

Should older adults be screened for dementia?

J. Wesson Ashford^{a,*}, Soo Borson^b, Ruth O'Hara^c, Paul Dash^d, Lori Frank^e, Philippe Robert^f,
William R. Shankle^g, Mary C. Tierney^h, Henry Brodatyⁱ, Frederick A. Schmitt^j,
Helena C. Kraemer^k, Herman Buschke^l

^aStanford / VA Alzheimer Center, Department of Psychiatry, Palo Alto VA Health Care System, Palo Alto, CA, USA

^bDepartment of Psychiatry, University of Washington, Seattle, WA, USA

^cDepartment of Psychiatry, Stanford University, Palo Alto, CA, USA

^dDepartment of Neurology, Johns Hopkins University, Baltimore, MD, USA

^eCenter for Health Outcomes Research, United BioSource Corporation, Bethesda, MD, USA

^fDepartment of Psychiatry, University of Nice, Nice, France

^gCognitive Sciences, U.C. Irvine, Irvine, CA, USA

^hGeriatric Research Unit, Sunnybrook and Women's College Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada

ⁱDepartment of Psychiatry, University of New South Wales, Sydney, Australia

^jDepartment of Neurology and Psychiatry, University of Kentucky, Lexington, KY, USA

^kDepartment of Psychiatry, Stanford University, Palo Alto, CA, USA

^lDepartment of Neurology, Albert Einstein College of Medicine, New York, NY, USA

Abstract

The question of whether to screen for dementia and Alzheimer's disease (AD) has been discussed in many forums throughout the world. Generally, medical advisory groups and policy-making groups have recognized the importance of early diagnosis but have uniformly avoided making recommendations to screen at-risk populations. This presentation reflects the support for reconsidering the importance of screening individuals at risk or above a certain age. In this statement, the majority of the authors support the consideration of dementia risk factors in individuals at age 50, with routine yearly screening after 75. Other authors remain concerned that the benefits of treatments of early disease do not yet support a general screening recommendation. These statements are made to encourage progress toward the development of a consensus regarding the widespread institution of screening policy. Accordingly, members of the worldwide scientific community are invited to add their perspective by contributing short commentaries (1500 words) on this subject. © 2006 The Alzheimer's Association. All rights reserved.

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1. Introduction

In an era of increasing capabilities to detect and manage prevalent disorders as early in their course as possible, screening has become an accepted approach for many medical conditions. Health professionals and the public accept screening for breast cancer, cervical cancer, colorectal cancer, diabetes, hypertension, high cholesterol, obesity, osteoporosis, and even for depression, provided treatment can be offered [1,2] Current US government announcements ad-

vise that Medicare covers the screening costs for all of these conditions [3]. However, screening for dementia, the most disabling common condition of later life [4], is currently left to chance. Further, estimates predict a three- to four-fold increase in dementia incidence and prevalence in the United States over the next 40 years [5]. The worldwide prevalence of dementia is forecast to double every 20 years, increasing from 24 million in 2001 to 40 million in 2020 and 80 million in 2040 [6]. Given several epidemiologic studies that suggest that some medical therapies might reduce the risk of dementia development (eg, nonsteroidal anti-inflammatory drugs [NSAIDs], statins), the growing availability of helpful symptomatic therapies, and initial research findings

*Corresponding author. Tel.:650-852-3287; Fax: 650-852-3297.

E-mail address: washford@medafile.com

that suggest potential to delay progression of mild cognitive deficits [7], routine screening for dementia warrants greater consideration.

Screening was defined in 1951 by the US Commission on Chronic Illness as:

“the presumptive identification of unrecognized disease or defect by the application of tests, examinations or other procedures which can be applied rapidly. Screening tests sort out apparently well persons who probably have a disease from those who probably do not. A screening test is not intended to be diagnostic. Persons with positive or suspicious findings must be referred to their physicians for diagnosis and necessary treatment” [8].

The definition of screening published by the UK National Screening Committee [9] differs in that it requires a condition of anticipated benefit that outweighs potential harm. In this screening is defined as: “a public health service in which members of a defined population, who do not necessarily perceive they are at risk of, or are already affected by a disease or its complications, are asked a question or offered a test, to identify those individuals who are more likely to be helped than harmed by further tests or treatment to reduce the risk of a disease or its complications.”

Detecting the presence of symptoms or signs of a disease does not require that formal diagnostic criteria be met. For dementia and its most common cause, Alzheimer’s disease (AD), screening is a means to identify the critical cognitive impairments or daily living dysfunctions that signify the earliest manifestation that can be recognized feasibly.

Screening is different from evaluation of risk factors, including genotyping [10,11]. In the future, disease biomarkers may be identified that can detect very early disease states, but these potential measures are still under development. Note also that the definition of screening differs from that of “case finding.” The Dictionary of Epidemiology definition of *case finding* includes: “secondary prevention through early detection of cases among persons using health services for other reasons, eg, checking blood pressures of all patients who attend a physician’s office” [8]. The UK-NSC defines *case finding* as “actively trying to diagnose probands for cascade screening,” which is “systematic identification and testing of members in a proband’s family” [9]. Screening is therefore an activity relevant to larger numbers of a population.

The UK-NSC lists the criteria for appraising the validity, effectiveness, and appropriateness of a “screening programme,” which include the nature of the condition and the availability of test(s) and treatment(s). With respect to dementia and AD, it may be conservatively contended that all of the UK-NSC criteria are met:

for “The Condition”: dementia and AD are clearly important health problems.

for “The Test”: there are many adequate tests that have been well studied for both dementia and AD screening.

for “The Treatment”: not only have several medications been approved by the US Food and Drug Administration (FDA) and other regulatory authorities for AD treatment and been shown by many studies to have beneficial effects, but there are other planning options and treatment modalities that are important for patients with early AD and other types of dementia that should begin as soon as possible.

2. Organization position statements on screening

In spite of the apparent need for screening programs for dementia and AD, many clinical experts [12,13] and organizations have stopped short of recommending such an approach. The following provides a listing of major organizations and their dementia or AD screening recommendations:

The US Preventive Services Task Force “concludes that the evidence is insufficient to recommend for or against routine screening for dementia in older adults,” citing a lack of evidence that screening improves outcomes [2,14]. This statement inappropriately attributes to screening the potential adverse effects of therapies. The only negative impact of a false-positive could be at most a brief secondary assessment to confirm or refute the results of the screen. It overlooks the fact that only diagnostic evaluation, not screening, bears the responsibility for guiding clinical treatment decisions.

The Agency for Healthcare Research and Quality (AHRQ then the AHCPR) calls for physicians to observe specific “triggers” that should initiate an assessment for dementia yet does not clearly define what those triggers are or propose a means by which physicians can learn to observe them. The AHRQ guideline does, helpfully, caution physicians to question any automatic attribution of obvious cognitive changes to aging alone [15].

The American Academy of Neurology strongly supports identification and active management of demented patients yet recommends against screening “unless cognitive impairment is (already) suspected” [16]. At that point, the problem is no longer one of screening but of confirmation of the already suspected case. As for the AHRQ recommendations, no means is proposed to improve clinicians’ ability to suspect dementia. This approach could obviously miss the earliest stages of disease.

The French agency, Agence nationale d’accréditation et d’évaluation en santé (French National Agency for Accreditation and Evaluation in Healthcare [ANAES]) [17], in their “Guidelines for Diagnosis of Alzheimer’s Disease,” provided only superficial recommendations to the general practitioner for improving the diagnostic consultation, specifically, “to define a strategy for diagnosis of a patient whose reason for consultation is a complaint about memory impairment or other symptoms suggesting a decline in cognitive function.” Like most organizations, this agency gave no advice as to how to deal with the fundamental problems

related to assessing cognitive status to discover impairments in mildly demented patients. General clinical experience is that dementia patients are nearly always unable to perceive the extent or significance of their own memory impairment by the time dementia has developed, so they do not usually complain about this loss. Further, families may avoid addressing the presence of cognitive impairments when they observe them in the affected individual and may even collude to prevent their recognition by others. Clinicians rarely take (or have) the necessary time to investigate subtle cognitive difficulties in elderly individuals and often miss warning signs such as missed appointments and failure to comply with prescribed medication regimens. In 2003, the ANAES provided no recommendation for general screening at the population level. However, between 2003 and 2005, the French Ministry of Health developed the Alzheimer's Disease Initiative (2003, 2005, and 2007 Action Plans) promoting the development of Memory Consultation and Research Memory Centers with the aims to improve the early diagnosis of AD and related disorders and to organize a network with general practitioners and other professionals involved in the field.

The North of England Evidence Based Dementia Guideline Development Group [18] specifically states, "population screening for dementia in the over 65s is not recommended; a case finding approach is recommended." This group expressed the clinical opinions that "complaints of memory impairment are not a good indicator of dementia," that "a history of loss of function is more indicative," and that "the general practitioner's judgment alone compares unfavorably with the use of formal cognitive testing in the diagnosis of dementia." Further, this group makes the additional recommendation, "general practitioners should consider using formal cognitive testing to enhance their clinical judgment." However, this group fails to recommend which tests to use and how often to use them throughout the elderly population at risk. Neither definition of *case finding* (as given above) appears to describe a method, as recommended by this group, which would substantially improve the discovery of dementia cases, either in early or middle stages. Although this group, in spite of its name, makes its recommendations based on the clinical opinions of general practitioners, recommendations based on evidence are given more weight by most US organizations [2].

The Canadian Consensus Conference on Dementia [19] suggests that, "there is insufficient evidence to recommend for or against screening for cognitive impairment in the absence of symptoms of dementia." This recommendation fails to specify how "symptoms of dementia" are to be identified. Although this conference also recommends "memory complaints should be evaluated and the patient followed up to assess progression," it avoided the issue that "memory complaints" may appear as late sequelae of memory problems, can result from dementia and other condi-

tions, and are usually reported by family members or other caregivers after a significant period of impairment or stress owing to the presence of cognitive impairment and personality changes associated with a dementing condition.

The Alzheimer's Association sponsored a Work Group on Screening for Cognitive Impairment and Alzheimer's Disease [20], which reviewed the principles of public health screening and carefully outlined concerns that should be addressed in developing a screening process for AD. While this group listed reasons for immediately beginning implementation of AD screening, they focused their report on cultural issues rather than making practical recommendations for initiating the screening process.

The Alzheimer's Foundation of America outlined reasons why memory screenings are important and described who should take such screening, and they have set up an annual screening event, "National Memory Screening Day" [21]. However, this organization has not developed appropriate dementia screening practices or a suitable system to manage positive results.

Excerpta Medica (sponsored by Pfizer Ltd) organized a UK nationwide educational program that included a series of 24 workshops for 990 participants including 270 general practitioners. These physicians supported either "formal" (whole or subpopulation) screening or "opportunistic" screening [22]. *Case finding* was not perceived as an alternative to screening.

3. Summary comment on organization positions

In general, the recommendations of the various organizations are *reactive* to the clinical situation of the patient who either self-identifies as having a problem or is brought to a clinician based on someone else's concern about loss of cognitive functioning. Such recommendations are missing the now evident need for early clinical and psychosocial interventions.

Central to each of these policy statements is the acknowledgement that physicians should be sensitive to evidence of cognitive impairment and should act on their suspicions. However, none of these official recommendations and policy statements clearly proposes a method whereby physicians are to develop such suspicions of cognitive impairment before dementia is *obvious* to all. Furthermore, the evidence strongly suggests that physicians, bombarded by demands for performance across increasing numbers of conditions and treatments, are not sufficiently sensitive to signs of cognitive impairment or early dementia [14,23,24]. Waiting to initiate dementia assessment until after dementia is suspected, particularly if based on a superficial observation of the progressive loss of daily living skills, delays diagnosis and symptomatic treatment

4. New operating definition of dementia screening

Screening is simply a paradigm for operationalizing the initial step in the discovery of significant cognitive impairment indicating at least mild dementing disease. A clear distinction must be drawn between screening and diagnosis [25,26]. There is already broad recognition of the value of early detection and treatment of dementia. There is extensive evidence of substantial under-recognition of dementia and AD from 50% to 80% even into moderate and severe stages and that screening would largely redress this gap [23,24,27–29]; those not obtaining a diagnosis will clearly not be receiving recommended and available treatments.

It is legitimate to insist that screening tests be properly validated [26,30], but it is equally important to not confuse screening tests with the diagnostic tests to which they lead. Screening must not be asked to bear the responsibility for negative consequences associated with a lack of available clinical expertise, supervision, and counseling [25] once dementia is identified. Consequently, the absence of empirical data on the specific impact of screening on patient outcomes is not sufficient to justify a decision to recommend against it. The reasonable approach is to decide what the criterion level should be for screening, given accepted estimates of the value of early detection and treatment, balanced against the costs of testing and false-positive results [31].

5. Why should routine screening be supported?

5.1. Rates of detection and diagnosis of dementia need to be increased

Physicians do not suspect dementia often enough, missing at least half the cases of mild and moderate dementia [14,27,28]. Recognition of dementia by primary care physicians is poor until it is at least moderately advanced [23,32]. There is ample evidence that screening can improve case identification [23,27], leading to the suggestion that community screening could double the number of patients diagnosed with dementia depending on the penetration of the screening system into local cultures [20,33,34]. Only the implementation of screening practices can rectify this failure of current diagnostic practices.

5.2. Early diagnosis could facilitate better treatment

Accepted management practices cannot be implemented for dementia patients until their condition is recognized. Dementia interferes with patients' abilities to carry out medical treatments, compromises treatment, and increases costs of managing other chronic diseases with demonstrated costs for comorbid conditions relative to those without dementia [35] and increases the use of the most expensive health care resources [36], including inpatient beds and emergency rooms. Improving overall management requires

modifying medical care plans to compensate for the effects of cognitive deficits. Increased cost burden (at the level of the patient, the insurer/government, and society) could be mitigated by early knowledge that cognitive impairment is present through improved vigilance by clinicians, caregivers, and patients.

5.3. FDA-approved medications may significantly delay decline in cognition, function, and nursing home placement

Although based on studies considered less reliable in design than randomized controlled trials (RCTs), data from pharmaceutical companies and pharmacy databases have suggested that the cholinesterase medications slow the rate of AD progression and delay nursing home placement [37–39]. Although all studies addressing this issue to date suffer from design limitations, their results are consistent with known clinical effects of drug therapy from randomized placebo-controlled trials. Further, numerous studies of several cholinesterase inhibitors and memantine have shown clinically significant, positive effects in patients who already have AD, with very few exceptions [40,41].

5.4. Early diagnosis is of considerable potential benefit for dementia caused by treatable etiologies (non-AD)

Of patients who have cognitive impairment or dementia owing to non-Alzheimer's disorders, approximately half of them have a cerebrovascular cause [42]. In many cases, proper risk factor identification and treatment of the underlying etiology of cerebrovascular disease can arrest or delay progression, such that screening makes early detection and preservation of functional abilities possible in these patients.

5.5. As part of early diagnosis recommendations, screening should already be considered an important concept to develop

Many policy authorities have already supported the case for diagnosing dementia at earlier stages than current practice achieves (see Organization Position Statements). To advance in this direction, there is a need to develop a method for operationalizing the initial step in the process; screening is that first step.

5.6. Screening is a useful, brief assessment and can initiate an important evaluation process

A brief screen frequently provides useful information about a patient's cognitive state to a clinician. Further, screening does not obligate clinicians to undertake a lengthy, expensive workup—it merely obligates them to take appropriate steps to determine whether a positive screen is likely to be true or false. The second step after an initial screen can be as simple as an expanded clinical history and a few questions asked of family members

[43,44]. Once a positive screen is supported, ample recommendations are available to guide physicians in pursuing an appropriate diagnostic evaluation [45–50].

5.7. *Screening for early dementia and early detection could avoid specific harms*

Dementia and AD are associated with diminishing ability to care for oneself and a considerable increase in potentially preventable accidents (eg, auto accidents, fires), injuries to self or others, property damage or loss, and complications of comorbid medical conditions [51]. Dementia also constitutes a risk for potentially preventable family violence [52]. Early recognition of dementia could identify individuals at risk for these avoidable harms and lead to interventions to reduce their incidence.

5.8. *A focus on screening will support public education and foster research*

As the focus on AD and understanding of its pathophysiology has increased, with many projects aiming to develop treatment and prevention methodology, a need has grown to recognize a greater number of patients at early stages to participate in research studies. Screening approaches will increase public awareness and bring the needed patients into research studies, accelerating the finding of treatments and preventive approaches.

6. What type of screening should be used?

Screening may be applied to a population (“mass,” “community,” “formal” screening), to a specific risk group (“prescriptive” screening), or to individuals who for other reasons come to a setting where screening might occur (“opportunistic” screening). Prescriptive screening has as its aim the early detection in presumptively healthy, but at-risk individuals of specific diseases that can be controlled better if detected early in their natural history. An example of prescriptive screening is the use of mammography to detect breast cancer [8]. An example of opportunistic screening is screening for diabetes in primary care practices. The purposes of screening for a particular condition determine which type is most appropriate.

With respect to dementia, screening should be targeted at those with sufficient risk to warrant the testing. Consequently, an important issue is how to determine a priori risk for individuals in a population. The most central risk factor for AD is age [11]. Other important risk factors are family history, genotype, and concurrent medical conditions. Given age and other variables, calculations can be made for any individual to determine when and how often they should seek screening. Opportunistic screening, only screening those individuals who come to a clinical office, would miss patients with mild but pathologic cognitive impairment or early dementia that avoids clinical encounters.

7. What level of screening test should be chosen?

The level of a test is the mean value of the probability of a positive test over all of the individuals in a population [31]. For the majority of patients, dementia onset is not sudden, and AD, responsible for more than half of all cases, is believed to be associated with an extensive presymptomatic or preclinical period of neuropathologic deterioration [53–57] before a vascular event or continued progression leads to its manifestation as dementia [58–64]. Further, early detection may be just as important or more so in early dementia stages related to etiologies other than AD (eg, vascular, B12 deficiency), where treatments may have more impact. Therefore, a critical issue is at what point along this early continuum of cognitive impairment should screening tests be calibrated to detect early dementia?

A controversy has arisen in the field regarding the construct of mild cognitive impairment (MCI) [16,65,66]. A recent definition of MCI is memory impairment without impairment of social function [67–69]. However, this definition lacks clinical precision, particularly with regard to the extent of cognitive impairment that distinguishes the MCI construct from normal aging and dementia. Further, there is concern with defining a state with cognitive impairment without functional impairment, because any cognitive impairment could be expected to be associated with some functional impairment if the assessment of function were adequately sensitive [43,70]. For example, a mild subjective memory difficulty would most likely be recognized because it had interfered with some complex function, which led to the concern. Also, subtle memory problems would be noticed at different levels depending on the individual’s functional demands, eg, repetitive labor versus complex analysis. Instead, these earliest, “preclinical” or “prodromal stages” [49] of dementia (including MCI) and particularly AD would be better viewed as occurring along a temporal continuum that emerges from the normal state [54,71–76]. The issue for screening is to recognize that emergence at the earliest time-point in the development of dementia or AD that is clinically helpful and cost effective.

Although several levels of analysis support the thesis that interventions should have the most impact when applied at the earliest possible point in the early progression of the disease [77–80], RCTs of antidementia medications have not provided data to support initiating treatment at the stage currently recognized as MCI [7,81]. The rationale for early recognition of dementia is stronger for other etiologies that would clearly benefit from early treatment (eg, vascular, normal-pressure hydrocephalus, B12 deficiency) is included. Scientific evidence has therefore not yet completely defined the transition point at which progression of a cognitive disorder justifies detection on the basis of treatment outcomes. Accordingly, screen development must continue to work toward instruments that function well for optimal

early recognition, because evidence about the best time to initiate treatment evolves through research.

8. What is the best screening test to use?

Many dementia screening tests have been developed and studied in numerous populations, using both prospective and retrospective analyses, and recommended for consideration [82–88]. Several screens have adequate sensitivity and specificity to serve as routine, cost-worthy evaluations [31]. Some studies [82,83,85,86,89–94] compare the performance of more than one candidate screen in the same sample in primary care or tertiary care or research settings; one study made the comparison in a population-based epidemiologic sample [90]. The major considerations in choosing a screening test are practicality and applicability in settings in which older adults receive their care.

Screening tests may be short cognitive tools administered to patients, high-sensitivity questions asked of patients themselves, questions asked of family members, or some combination of all of these approaches. There is evidence that informant questionnaires perform as well as brief cognitive tests for detection [44] and combinations may enhance detection rates [71,93,95]. In the future, computerized tests are likely to be part of the screening process [96,97], and telephone-based tests may also play a role [98,99]. Any screening test with adequate sensitivity and specificity and reasonable cost should improve the likelihood that a dementia case is identified in a timely manner. Several comparative reviews on the application of screening tests for dementia and AD are available [100,101].

In considering the development of progressively better screening tests for the future, it is necessary to understand the underlying pathology that leads to dementia, particularly AD, and how knowledge of its effect on the brain can be translated to effective recognition of early changes [102]. The fundamental brain memory mechanism, neuroplasticity, is the core process disrupted in AD [71,103]. Therefore, cognitive screens must address memory at a minimum and may include other components of cognition as well as questions that specifically concern those types of social or occupational function that are most dependent on the formation of memory traces [43,44,104]. Even at very mild levels of cognitive impairment, patients and family members can discern behavioral changes and impairments in personality that are associated with subsequent dementia [105,106] and in a range of everyday functional abilities [70,91]. Further, numerous steps still need to be taken to accommodate the broad cultural and educational backgrounds of elderly individuals [20,33,34,107]. However, it is important to recognize such concepts as guides for further development of screening test content, not as an impediment to the immediate use of available tests, which, are already greatly needed. Finally, with the development of disease-specific

biomarkers, disease presence may eventually be detected long before significant neural degeneration has occurred.

9. At what age should screening begin?

In principal, public policy concerning screening should be grounded on the cost worthiness of the screening process [31]. Cost worthiness relates to properties of the screening test (ie, sensitivity, specificity, testing cost), the financial effects of the test (ie, benefits of a true-positive finding, costs of a false-positive finding), and the epidemiology of dementia. The incidence of AD is well known to be related to age [108–110], with the incidence rate doubling about every five years, passing 0.1% per year at about age 61 years, 1% at age 78, and 10% at age 96 [10]. Incidence values for MCI, if it is considered prodromal dementia or very early AD, should be greater than those for dementia and AD and shifted to a five-year younger age continuum [111]. Screening decisions should be based on the prevalence and incidence estimates for a population and be modified by certain individual risk factors such as family history, comorbid conditions associated with cognitive impairment (eg, diabetes, blood pressure, cardiovascular disease), and other risk factors [11,112,113]. Given relatively conservative estimates of the benefits of early diagnosis, justification can be made for yearly screening to begin by age 75, when most estimates of population annual incidence of dementia approach 1% [108,114–116]. At the 1% incidence level, the benefit of a true-positive diagnosis would only have to outweigh the cost of secondary assessments from a false-positive screen by a factor of 100 to justify inexpensive screening, and, after this age, the justification would be progressively greater. However, it may also be reasonable to discuss this issue with patients on a case-by-case basis, beginning at 50 years of age, to determine risk factors, particularly family history, and initiate a plan as to what age to begin regular screening. Regular screening could then be “informed” in those patients with elevated risk, possibly every year or every two years, and could reflect the base rates of dementia in a given clinical practice [117,118]. Repeated screening may be indicated more frequently if certain risk factors or warning signs develop. Ultimately, of the diagnostic criteria for dementia (A through E in Diagnostic and Statistical Manual, 4th revision [DSM-IV]), the most important sign for screening purposes is “C. The course is characterized by gradual onset and continuing cognitive decline” [71,119], which must be measured with respect to local norms and longitudinally against a person’s own prior performance.

10. Directions for future research

Several issues require further development as widespread screening is implemented [20]. The relative value of specific screening methods has not yet been established by

ongoing research. Successive formal recommendations should be progressively improved based on empirical data. It is likely that screening tests will evolve to utilize computerized testing then to the direct examination of disease-related biomarkers. The ethical and practical implications of self-screening versus limiting screening to a medical encounter require more attention [26].

Quantifying the impact of screening for dementia on individuals, family members, insurers, and society requires attention not just to cost or cost effectiveness but to a range of variables. A broad picture must be viewed to assure that measures that will benefit the greater good of society will not become unbearable costs for any specific social agency or group of individuals [78,120]. The absence of empirical data on the fiscal impact of screening is problematic and must be rectified. In particular, the pharmaco-economic definition of the financial benefit of treatment [35,121–123] will drive the development of screening systems directly.

As progressively more effective screening is implemented, diagnosis of dementia will be made earlier in the course, even to the point at which memory function is still essentially within the normal range. This advance will lead to development of early treatment trials and early treatments to preserve cognitive function. The ultimate goal of dementia prevention will likely be achieved by predicting who will have dementia and providing primary preventive interventions. Even if most dementia can eventually be avoided, screening will still be required to detect at the earliest stages those cases that have not been prevented.

11. Summary

Screening for cognitive impairment to identify early signs of dementia and AD should be considered for inclusion as a routine part of care for older adults, especially when dementia risk factors are identified. It is feasible to begin implementing screening practices now, particularly because the critical components of dementia management are currently established. While the field debates which outcomes are the most appropriate to define dementia policy overall and develops the appropriate measures and evidence base, we must not neglect the many demented patients whose care now suffers for want of recognition, treatment, and management. Continuing to defer routine cognitive evaluation or dementia screening of older adults denies care to the many patients who would benefit from early diagnosis. The field has now matured to the point at which routine screening of individuals at risk or above a certain age would likely improve clinical care and foster the advancement of research to reduce the impact of the terrible conditions causing dementia, including AD and other dementing disorders.

Dementia presents a challenge that requires further empirical clarification of the relationship between a screening result and the diagnosis of a progressive disorder. The science of screening can help by contributing the concept of the diagnos-

tic threshold and “test level.” Studies based on formal understanding of screening science can help resolve the questions of where the transitions from normal function, through MCI, to dementia are occurring. Advances in diagnostic standards will influence the development of screening processes; screening systems will likely influence diagnostic nosology. Improvements in screening and nosology will likely lead to more effective prevention and treatment programs.

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All of the authors have been associated with the development of screening tools for dementia and Alzheimer's disease. Dr Ashford is on the Speaker's Bureau for Janssen / Ortho-McNeil Pharmaceuticals. Dr Borson is a member of the Speaker's Bureau for Pfizer Pharmaceuticals, Forest Laboratories, and Novartis and has received investigator-initiated research funding from Pfizer, Forest, and Janssen Pharmaceutica and a conference grant from Eisai. Dr. Shankle is on the speaker's bureaus for Novartis and Ortho-McNeil Pharmaceuticals, and is currently chief medical officer of Medical Care Corporation.

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