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Should older adults be screened for dementia? It is important to screen for evidence of dementia!

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Abstract

Multiple arguments for considering routine dementia screening have been presented. Furthermore, dementia diagnoses are widely unrecognized. As a result, persons with dementia are missing important clinical care and treatment interventions. By distinction, the problems of defining, diagnosing, and treating mild cognitive impairment (MCI) are not yet resolved, and MCI is not ready for a screening recommendation. Dementia screening approaches, including cognitive testing and functional assessment, must be evaluated on their scientific merits, including sensitivity and

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Editor's Note: This paper was written in response to a comment submitted to this Journal on the consensus statement by a group of scientists concerned about screening for dementia, which was published in this Journal in April 2006 [1]. The submitted manuscript was withdrawn after this response was submitted. However, this response is being published because it addresses concerns about screening recommendations and provides clarification and additional information on key points concerning dementia screening.

specificity for recognizing affected individuals in at-risk populations. Screening tests must be "cost-worthy", with the benefits of true-positive test results justifying the costs of testing and resolving false-positive cases, with due consideration for proper diagnostic evaluation and potential harms. With the tremendous number of new cases projected in the near future and the expected emergence of beneficial therapies, considerably more research is needed to develop more efficient screening systems.

Keywords

Dementia; Alzheimer's disease; Screening; Diagnosis; Case-finding; Mild cognitive impairment

1. The clinical evidence justifies screening for dementia

In April 2006, a group of clinicians and scientists concerned about dementia screening [1] presented their consensus that screening at-risk populations for evidence of dementia was an important matter to consider (A&D Consensus Group). The A&D Consensus Group addressed the well-documented and widely recognized problem of inadequate recognition of dementia in clinical practice [2–6]. Freund [7] estimated that the missed diagnoses are greater than 25% of the dementia cases and might be as high as 90%. Dementia exerts a substantial burden on patients' lives and the lives of those close to them [8]. The A&D Consensus Group reviewed the responses of numerous national and international organizations to this worsening crisis and noted that none recommended screening for dementia, although essentially all of the reviewed organizations did recommend a diagnostic evaluation when memory problems or dementia were suspected. It is commonly accepted that most dementia patients are cared for in the primary care setting, and clinicians working in this setting do not have adequate time for in-depth consideration of unrecognized cognitive difficulties that their patients might have. Furthermore, there are a variety of reasons that the clinicians, the patients, and those close to the patients do not express concerns about the presence of dementia when symptoms are first noticed. Multiyear delays from first symptom occurrence to clinical assessment have been documented and attributed mostly to uncertainty about the severity of the cognitive deficit (47%) and attributing observed changes to normal aging (37%) [9].

To respond to the acknowledged need to improve recognition of dementia in primary care settings, the A&D Consensus Group recommended a systematic approach to enhancing suspicion of dementia that would otherwise go unnoticed. Accordingly, the A&D Consensus Group recommended that the process for suspecting and recognizing possible early dementia be carried out. The process required to detect unrecognized or unacknowledged disease is commonly referred to as screening. Given the abundance of adequate tests for recognizing mild dementia, the numerous benefits in doing so, the slight costs associated with such testing, and the minimal nature of the potential harms from such investigation (Table 1), this group recommended the consideration of implementation of procedures to screen for dementia. The perspective that it is reasonable to recommend screening for dementia has only recently developed and has been championed independently by other groups [10–12].

2. Defining the dementia-related conditions for screening consideration

There is a long-term problem in the field of dementia of defining the basic diagnostic issues and symptom constellations. The American Psychiatric Association (APA), during the prolonged period of development of the Diagnostic Manual, versions III and IV (DSM-III, DSM-IV), has established a diagnostic spectrum of dementia, including "Dementia of the Alzheimer Type," "Vascular Dementia," and "Dementia Due to Other General Medical Conditions" [13]. The core description of dementia includes development of multiple cognitive

deficits, including memory and other disturbances, causing impairment in social or occupational functioning. Generally, dementia does not have a defined onset, and the rate of progression varies extensively. The dementia course might be "characterized by gradual onset" that progresses insidiously, as is typical with Alzheimer's disease, or it might begin suddenly and progress in discrete increments, as might be seen with vascular dementia. The uncertainty of the point of dementia onset is one of the basic reasons that a screening system is needed; with a variable course, early dementia is difficult for clinicians to notice. There are now many widely acceptable management interventions that are not properly applied because the presence of the disease is missed. Because of the difficulty in recognizing this problem, along with the perceived value of recognition, many scientists and clinicians have sought to develop screening tests for this difficult problem.

Recently, there have been increasing discussions and extensive considerations of what follows normal function but precedes dementia, a concept now widely referred to as mild cognitive impairment (MCI) [14]. Although MCI has received a considerable amount of research attention, it has not been formally defined as a diagnostic entity for routine clinical purposes. MCI is being characterized as an early clinical stage of diseases that lead to dementia. Although MCI is of considerable academic and research interest, the core issue in primary care is early detection of Alzheimer's disease and related disorders, because the benefits afforded are considered to be substantial. From a purely pragmatic perspective, primary care physicians are not likely to have the time to know when a patient crosses the line from having MCI to having mild dementia, so that the physician's focus should simply be on detecting early dementia. Simple screening tests have not yet been developed to recognize or detect MCI [15], although there are a few tests that accurately distinguish normal aging from MCI [16] at levels comparable to tests for other conditions for which screening is widely accepted, such as breast cancer and Down syndrome.

3. Reviewing the screening principles

Because dementia has been such a difficult syndrome to recognize in the primary care setting when symptoms are mild, it is important to use the best available screening principles to decide how to evaluate a subject for this problem. It is the contention of the A&D Consensus Group that all of the criteria for conducting a screen for dementia (as opposed to MCI) are met. This is a brief review of those principles for dementia:

3.1. It must be common

Dementia is admittedly very common, but it must also be noted that the prevalence increases steeply with age, more so than mortality [18]. As yearly incidence increases with age, the imperative to screen increases proportionally. Depending on ancillary considerations, the threshold for recommending routine screening to the population might be reached by age 75 years.

3.2. It must have sensitive and specific tests available for its detection

There are an abundance of tests available for dementia screening whose sensitivities and specificities that are acceptable for dementia screening purposes [10,15].

3.3. It must have efficacious treatment

There are five Food and Drug Administration–approved medications for Alzheimer's disease as well as recommended treatments for several other types of dementia. There are a few groups who have questioned the efficacy of the cholinesterase inhibitors for Alzheimer's treatment (originally Ashford et al [19]), and the most prominent has been the statement of the National Institute for Health and Clinical Excellence (NICE) in Great Britain in response to data from

Courtney et al [20]. The NICE appraisal was revised in November 2006 to include a recommendation for subsidizing use of cholinesterase inhibitors for moderately demented patients with Alzheimer's disease [21]. However, the preponderance of the studies have shown that the approved dementia medications have useful benefit for many patients [11,22,23]. Beyond specific treatments for Alzheimer's disease, there are efficacious biologic, psychological, and social interventions that should be at least considered as soon as possible in the Alzheimer's disease course and the types of dementia associated with other etiologies.

3.4. If treatment exists, treated patients must have better outcomes than untreated patients

As noted earlier, there has been some debate about this point, but many studies have shown the benefits of the treatments on biologic (brain scans), psychological (cognitive testing and behavioral testing), and social (ADLs, activities of daily living) measurements [11,22]. Furthermore, there are many types of dementia beyond Alzheimer's disease in which a specific early intervention is clinically superior to no intervention. Beyond specific clinical outcomes, the value of general supportive care for dementia patients and their families are outcomes that are being studied, and these outcomes must be included in the evaluation of the criteria for judging screening tests. Several studies have shown better outcomes for caregivers of treated patients, and these outcomes add further value to dementia screening.

3.5. The benefits from screening must outweigh the harms

There are multiple benefits and comparatively few and minor harms associated with the administration of specific screening tests for dementia (Table 1). The issue of harmful side effects from treatment is not directly related to screening. Instead, the cost-benefit of implementing treatments is a decision that is made on the basis of the diagnostic evaluation, independent of the rationale for initiating the diagnostic work-up. There is a concern that some clinicians may equate a positive screen with diagnosis, rather than making the proper secondary enquiries and initiating the diagnostic evaluation only when indicated; education for appropriate implementation and patient communication for screening is essential to address this quality of care issue.

For Alzheimer's disease, the side effects from the available treatments are usually manageable clinically. The concern that there might be increased mortality with the use of cholinesterase inhibitor treatment in patients with MCI is not directly germane to the issue of treating patients with diagnosed dementia of the Alzheimer type. However, the question of harms of treatment does introduce the issue that screening tests need to be followed by appropriate diagnostic evaluation before treatments are initiated. In addition, some other effects of cholinesterase inhibitors might have clinical benefit (eg, reduced constipation, slower heart rate, and improved behavior).

4. The need to distinguish the concepts of dementia and MCI

An important distinction must be drawn between dementia and MCI. MCI is a prodromal condition to dementia in many cases, but it is not a diagnosis of dementia. Screening for dementia is addressing a problem that has already been recognized by numerous official entities as requiring a diagnosis. In spite of popular interest in screening for MCI [17] and widespread concern about MCI in primary care practice, diagnostic criteria for MCI still need clarification, as was noted in the original A&D Consensus Group article. Further research is needed on screening methodology and treatment benefits before population screening for MCI will be ready for consideration. This concern applies to MCI screening, not to dementia screening as discussed in the A&D Consensus Group article.

5. Delineation of screening-related risks from adverse consequences of diagnosis

It is important to distinguish the risks involved in a screening test from the results that might occur as the direct outcome of clinical care. These factors include the potential adverse consequences of diagnostic tests and treatments. In the “Guidelines and Recommendations about Screening” [24], there are diagrams describing systems to implement screening tests; this article does not apply to dementia screening as discussed by the A&D Consensus Group because it presents a direct advance from screening tests to treatment. What is discussed in the A&D Consensus Group article is screening tests to determine when diagnostic tests should be considered. It is an adverse development if the results of any of the dementia screening tests are interpreted wrongly as a diagnosis of “Alzheimer’s disease” without proceeding through the Standard of Care diagnostic procedures for dementia diagnosis. Furthermore, the routine dementia diagnostic tests, including progressively: history and physical examination, blood tests, focused neuropsychological assessment, and a brain scan, are generally safe. However, it is reductionistic to indiscriminately apply the logic of attributing the numerous potential adverse consequences of complex clinical interventions to the use of a brief check for early dementia signs for triggering a complete evaluation.

After clarifying the separation of screening and diagnostic procedures, the correct point about screening tests needs to be reiterated, as expressed in the original Consensus Group statement, “The only negative impact of a false positive could be at most a brief secondary assessment!” In this circumstance, a screening test only leads to a recommendation of a second step in assessment. Such a test should be considered to be of no greater consequence than the commonly used screening question, “Do you have a cough?” for which the positive response should lead to auscultation of the lungs, not diagnosis and treatment of lung cancer. Thus, a dementia screening test by itself should carry limited social, psychological, or ethical concerns.

There is a related commonly expressed issue suggesting that a screening test can result in “labeling.” Labeling should not occur without a diagnosis. Because screening does not provide a diagnosis, there is no reason for labeling to occur. There have been appropriate concerns raised about psychological and social consequences of making a diagnosis of Alzheimer’s disease. This concern is appropriate and needs to be addressed as part of the refinement of dementia diagnosis. However, this is not a problem that should be related to appropriate screening. Accordingly, education should accompany screening implementation to delineate limitations of screening clearly and to outline the appropriate uses of derived information.

Another concern is that individuals participating in a screening test would make inappropriate decisions about the recommendations resulting from the testing. Failure of a subject with a positive screen to get further diagnostic assessment is a concern, but compliance with medical recommendations is a widespread problem, not just related to screening tests. Compliance problems represent one of the points in which modern medicine needs broad-based improvement that appears to be difficult to address within an overburdened health care system. The opposite problem, that an individual with a negative screen might see this result as permanent freedom from worry about dementia, is also a concern and a misunderstanding. The negative screening result only suggests that the concern about dementia can be reduced for a limited period of time, for example, 1 year. Such inappropriate patient responses to screening test results should not be considered harms of screening but areas for attention and patient education in which the quality of the whole screening system could be progressively improved, and population education can lead to an overall improvement in the health of society.

6. Financial costs associated with screening

There are monetary costs incurred by screening and the resulting increase of care burden. Analyses of this issue should formally address the "cost-worthiness" of the medical test [25]). Such analyses have been reported and published [11], and looking at limited health economic data, the results tend to support screening. However, the A&D Consensus Group further argued that the benefits from having information about mental dysfunction can help the patient's support system function more efficiently and with less stress and plan for more effective management of the issues that will develop as the patient deteriorates.

7. Conclusions

1. In the development of cognitive and memory screening tests, a clear distinction must be drawn between screening for dementia and screening for MCI. Tests are currently available that should be considered cost-worthy for dementia screening. The basis for screening for MCI is not yet established.
2. The decision to screen for dementia should be based on sound scientific consideration of all relevant issues and public health benefits, not political issues. Further attention to dementia screening is clearly warranted, although implementation will require careful development of practice guidelines and public education that might vary considerably across different settings.
3. Dementia screening in clinical settings is clearly appropriate for those whose risk is above a certain threshold, for example, persons older than the age of 75 years. Widespread screening of the whole elderly population also has merit, although systematic recommendations need to be developed. Full public health screening will become justifiable when more substantive therapeutic and/or preventive interventions are developed, and such therapies are currently under intense testing. Consequently, now is the time to prepare for the future by developing dementia screening systems and memory testing programs that will be able to detect patients with early phases of dementia.

8. Addendum

8.1. Motivations of professionals in the field of dementia screening

A concern is always present about whether there are irreconcilable conflicts of interest when recommendations are made with broad social implications, in this case, either to screen or not to screen for dementia. There are financial and professional incentives that operate in all human beings. Financial motivations are clear for the pharmaceutical industry. However, as is apparent from problems that certain pharmaceutical companies have had recently, attempts to obtain results in violation of accepted ethical principles for scientific conduct lead to direct financial risk and harm to company reputation with attendant financial consequences. More often and more profitably, pharmaceutical companies do their best to follow all of the rules very carefully, although at least in part because of the careful scrutiny. Furthermore, all scientists, even the peer reviewers at the National Institutes of Health, have their own issues and biases, and they are working in a political arena that also is fraught with personal ambitions. The co-authors of the original article are admittedly those interested in screening test development. That interest is a direct result of their interest in providing optimum care for patients. The motivations of all parties involved in making comments that can influence social policy need to be similarly scrutinized.

8.2. Notes about potential conflicts of interest for funded or unfunded researchers

Opinions of funding organizations cannot be taken as accepted opinions of all of those funded by those organizations. Simply because a group has received funding for their research from various organizations, some of which may support or are opposed to screening, does not mean that opinions expressed by them are biased by those organizations. Similarly, opinions or implicit agendas of funding organizations associated with the A&D Consensus Group do not necessarily bias the expressed opinions.

References

1. Ashford JW, Borson S, O'Hara R, Dash P, Frank L, Robert P, et al. Should older adults be screened for dementia? Alzheimer's & Dementia 2006;2:76–85.
2. Callahan CM, Hendrie HC, Tierney WM. Documentation and evaluation of cognitive impairment in elderly primary care patients. Ann Intern Med 1995;122:422–429. [PubMed: 7856990]
3. Ross GW, Abbott RD, Petrovitch H, Masaki KH, Murdaugh C, Trockman C, et al. Frequency and characteristics of silent dementia among elderly Japanese-American men: the Honolulu-Asia Aging Study. JAMA 1997;277:800–805. [PubMed: 9052709]
4. Sternberg SA, Wolfson C, Baumgarten M. Undetected dementia in community-dwelling older people: the Canadian Study of Health and Aging. J Am Geriatr Soc 2000;48:1430–1434. [PubMed: 11083319]
5. Valcour VG, Masaki KH, Curb JD, Blanchette PL. The detection of dementia in the primary care setting. Arch Intern Med 2000;160:2964–2968. [PubMed: 11041904]
6. Finkel SI. Cognitive screening in the primary care setting: the role of physicians at the first point of entry. Geriatrics 2003;58:43–44. [PubMed: 12813873]
7. Freund B. Office-based evaluation of the older driver. J Am Geriatr Soc 2006;54:1943–1944. [PubMed: 17198503]
8. Frank L, Lloyd A, Flynn JA, Kleinman L, Matza LS, Margolis MK, et al. Impact of cognitive impairment on mild dementia patients and mild cognitive impairment patients and their informants. Int Psychogeriatr 2006;18:151–162. [PubMed: 16403246]
9. Knopman D, Donohue JA, Gutterman EM. Patterns of care in the early stages of Alzheimer's disease: impediments to timely diagnosis. J Am Geriatr Soc 2000;48:300–304. [PubMed: 10733057]
10. Solomon PR, Murphy CA. Should we screen for Alzheimer's disease? A review of the evidence for and against screening Alzheimer's disease in primary care practice. Geriatrics 2005;60:26–31. [PubMed: 16287338]
11. Fillit HM, Smith Doody R, Binaso K, Crooks GM, Ferris SH, Farlow MR, et al. Recommendations for best practices in the treatment of Alzheimer's disease in managed care. Am J Geriatr Pharmacother 2006;4:S9–S24. [PubMed: 17157793]
12. Chopra A, Cavalieri TA, Libon DJ. Dementia screening tools for the primary care physician. Clinical Geriatrics 2007;15:38–45.
13. American Psychiatric Association. Diagnostic and statistical manual, IV. Arlington, VA: American Psychiatric Association; 1994.
14. Petersen RC. Mild cognitive impairment as a diagnostic entity. J Intern Med 2004;256:183–194. [PubMed: 15324362]
15. Schmitt FA, Mendiondo MS, Kryscio RJ, Ashford JW. A brief Alzheimer's screen for clinical practice. Res Pract Alzeimer's Dis 2006;11:1–4.
16. Trenkle D, Shankle WR, Azen SP. Detecting cognitive impairment in primary care. performance assessment of three screening instruments. J Alzheimer's Disease. [in press].
17. Dale W, Hougham GW, Hill EK, Sachs GA. High interest in screening and treatment for mild cognitive impairment in older adults: a pilot study. J Am Geriatr Soc 2006;54:1388–1394. [PubMed: 16970647]
18. Raber J, Huang Y, Ashford JW. ApoE genotype accounts for the vast majority of AD risk and AD pathology. Neurobiol Aging 2004;25:641–650. [PubMed: 15172743]
19. Ashford JW, Soldinger S, Schaeffer J, Cochran L, Jarvik LF. Physostigmine and its effect on six patients with dementia. Am J Psychiatry 1981;138:829–830. [PubMed: 7246817]

20. Courtney C, Farrell D, Gray R, Hills R, Lynch L, Sellwood E, et al. Long-term donepezil treatment in 565 patients with Alzheimer's disease (AD2000): randomised double-blind trial. Lancet 2004;363:2105–2115. [PubMed: 15220031]

21. National Institute for Health and Clinical Excellence (NICE). NICE technology appraisal guidance 111. donepezil, galantamine, rivastigmine (review) and memantine for the treatment of Alzheimer's disease, includes a review of NICE technology appraisal guidance 19. London, UK: 2006.

22. Geldmacher DS, Frolich L, Doody RS, Erkinjuntti T, Vellas B, Jones RW, et al. Realistic expectations for treatment success in Alzheimer's disease. J Nutr Health Aging 2006;10:417–429. [PubMed: 17066215]

23. Tinklenberg JR, Kraemer HC, Yaffe K, Ross L, Sheikh J, Ashford JW, et al. Donepezil treatment and Alzheimer's disease: can we apply the results of randomized clinical trials to AD patients in clinical practice? Amer J Ger Psych. 2007 [In press].

24. Barratt A, Irwig L, Glasziou P, Cumming RG, Raffle A, Hicks N, et al. Users' guides to the medical literature: XVII. How to use guidelines and recommendations about screening: Evidence-based Medicine Working Group. JAMA 1999;281:2029–2034. [PubMed: 10359392]

25. Kraemer, HC. Evaluating medical tests. Newbury Park, CA: Sage Publications, Inc.; 1992.

26. Molnar FJ, Patel A, Marshall SC, Man-Son-Hing M, Wilson KG. Clinical utility of office-based cognitive predictors of fitness to drive in persons with dementia: a systematic review. J Am Geriatr Soc 2006;54:1809–1824. [PubMed: 17198485]

Table 1

Benefits and harms of dementia screening

- Psychological and social benefits from early dementia recognition
  - Early education of caregivers on how to handle the patient
  - Advance planning while patient is competent, establishing a will, proxy, power of attorney, advance directives
  - Reduced patient and family anxiety, uncertainty, and stress and improved family understanding of demented patient, reduced caregiver burden, blame, denial
  - Promote safety in driving, medication compliance, cooking, etc
  - Patient's and family's right to know especially about genetic risks
  - Promote advocacy for research and treatment development
- Medical benefits from early dementia recognition [11,22]
  - Early diagnosis and treatment and appropriate intervention might improve overall course substantially, including lessening disease burden on caregivers and society
  - Specific treatments are now available for Alzheimer's disease (anti-cholinesterases, memantine). These medications have been shown to:
    - Temporarily improve cognitive dysfunction
    - Temporarily improve function (ADLs)
    - Delay conversion from MCI to Alzheimer's disease
    - Decrease development of behavior problems
    - Delay nursing home placement
- Harms from failure to recognize early dementia
  - Dangerous behaviors: cooking, operating machinery
  - Driving problems [26]
- Listing and accounting for the harms of not screening for dementia [12]
  - Missed opportunities for:
    - the application of available treatments
    - participation in research
    - advance care planning
    - support of caregivers
- Listing and accounting for the harms of dementia screening [24]
- Harms that might occur to those with positive screening test result
  - Clinical error of equating positive screen with diagnosis (education about screening and proper dementia diagnostic implementation can address this issue).
  - Complications arising from further testing (only additional clinical questions necessary to inquire about the patient's history should be considered at this point, as is recommended for evaluation of suspicion of dementia by the AAN).
  - Adverse effects of treatment must be considered with respect to the benefits, on their own merits, based on the opinion of the clinician that makes the decision for treatment.
  - Anxiety generated by investigation and treatment; such anxiety must be balanced against the already considerable and appropriate anxiety about Alzheimer's disease in our society. Screening in the context of proper diagnosis and medical management can help manage that anxiety.
  - Costs and inconvenience incurred during evaluation; the cost of dementia evaluation needs to be entered in the calculation of whether screening is cost-worthy
- Harms that might occur to those with negative screening test result

False reassurance: a false negative might wrongly diminish concern and motivation to participate in future evaluation. The consequences of incorrect results are factors that can be accounted for in the decision to screen.

Abbreviations: ADL, activities of daily living; AAN, American Academy of Neurology.