19: Recognition and Initial Assessment of Alzheimer's Disease and Related Dementias

Clinical Practice Guideline No. 19.

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Guideline Development and Use

Guidelines are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical conditions. This guideline was developed by a private-sector panel convened by the Agency for Health Care Policy and Research (AHCPR). The guideline reflects the state of knowledge, current at the time of publication, on effective and appropriate care.

The panel employed an explicit science-based methodology and expert clinical judgment to develop specific statements on patient assessment and management for the clinical condition selected. Extensive literature searches were conducted, and critical reviews and syntheses were used to evaluate empirical evidence and significant outcomes. Peer review was undertaken to evaluate the reliability and utility of the guideline in clinical practice. The panel's recommendations are primarily based on the published scientific literature. When the scientific literature was incomplete or inconsistent in a particular area, the recommendations reflect the professional judgment of panel members and consultants.

We believe that this AHCPR-assisted clinical practice guideline will make positive contributions to the quality of care in the United States. We encourage practitioners and patients to use the information provided in the guideline. The recommendations may not be appropriate for use in all circumstances. Decisions to adopt any particular recommendation must be made by the practitioner based on available resources and circumstances presented by individual patients.

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Publication of this guideline does not necessarily represent endorsement by the U.S. Department of Health and Human Services.

Abstract

Dementia in the adult U.S. population is a devastating disorder that is often unrecognized or misdiagnosed in its early stages. Despite the current lack of unequivocally effective treatment, recognition of early-stage dementia may offer substantial benefits. These include avoidance of inappropriate treatment related to misdiagnosis and time for the patient and family to address issues of financial, legal, and medical care planning.

This *Clinical Practice Guideline* is intended to help primary care providers recognize and assess Alzheimer's disease and related dementias in their early stages. Differential diagnosis is beyond the scope of the guideline; however, the guideline contains a list of resources for further clinical evaluation once probable dementia has been identified.

Guideline recommendations focus on the following areas:

- Triggers that should prompt a clinician to undertake an assessment for early-stage dementia.
- The components of an initial assessment, including tests of mental status and functional performance.
- A flow chart for early recognition and initial assessment, including assessment for delirium and depression.
- Interpretation of test results and appropriate actions.
- The role of neuropsychological testing.

Knowledge of the individual patient is emphasized, including change in ability from baseline, as is the value of reliable informant reports to initial assessment and clinical judgment.

This guideline should help clinicians recognize symptoms of possible dementia and decrease underrecognition and misdiagnosis of this devastating condition.

Acknowledgments

Many people and professional organizations contributed importantly to the development of this *Clinical Practice Guideline,* from its earliest stages through two review cycles. The consultants, technical advisors, and reviewers listed at the end of this guideline devoted considerable time and effort to this collaborative effort and greatly helped the panel. Several persons helped immeasurably in identifying key issues, compiling relevant literature, and critiquing manuscript drafts of the guideline. These persons were Alan Zonderman, PhD, and Jeffrey Herbst of the Gerontology Research Center, National Institute on Aging; Andrea Pinkham of the University of Iowa; and Gary VandenBos, PhD, executive director of publications and communications, American Psychological Association.

Special acknowledgment goes to Mark Somerfield, PhD, who served with great dedication and competence as project coordinator, overseeing the literature reviews and data coding and extraction for the meta-analyses and without whom this guideline would not have been possible.

The methodological and statistical expertise of Lawrence Hedges, PhD, of the University of Chicago, and Victor Hasselblad, PhD, of Duke University School of Medicine, made possible the meta-analyses that led to several of the guideline's key recommendations.

The Cochairs also thank Barbara J. Shapiro, panel editor, for her superb writing and editing skills and Carole Sherman, panel manager, for her deft supervision of the support services provided by Technical Resources International, Inc. Finally, thanks are due to the Agency for Health Care Policy and Research for its continuing support of the panel's work and its commitment to an evidence-based approach to improving clinical practice.

Executive Summary

Dementia is a syndrome of progressive decline that relentlessly erodes intellectual abilities, causing cognitive and functional deterioration, which leads to impairment of social and occupational functioning. After onset, many patients live a decade or more with advancing debility. Alzheimer's disease and related dementias affect at least 2 million, and possibly as many as 4 million, U.S. residents. The direct and indirect costs to society and affected

families are massive: the National Institute on Aging estimates that $90 billion is spent annually for Alzheimer's disease alone. The noneconomic toll is incalculable.

Rates of dementia increase with advancing age. Studies have found consistent evidence for only two other risk factors: family history of dementia and presence of Down syndrome. For Alzheimer's disease, recent research has identified at least three autosomal-dominant forms, all with early-onset symptoms, involving chromosomes 1, 14, and 21. Alleles of the apolipoprotein E 4 gene locus on chromosome 19 have been associated with late-onset Alzheimer's disease.

Alzheimer's disease is the most prevalent dementing disorder in the United States, followed by vascular dementia. Among the other causes of dementia are Parkinson's disease, Huntington's disease, progressive supranuclear palsy, and amyotrophic lateral sclerosis (ALS, often referred to as Lou Gehrig's disease).

The difficulties of correctly diagnosing dementia in its early stages have been documented. In some cases, clinicians diagnose dementia or Alzheimer's disease where it does not exist; in others, a dementing disorder is misdiagnosed or unrecognized. One explanation is a tendency to regard mild deficits of early-stage dementia as inevitable consequences of aging. Despite the acknowledged difficulties of diagnosing early-stage dementia, however, a number of characteristics distinguish it from normal aging and from other syndromes that involve cognitive problems.

Although research on dementia is advancing rapidly, the current medical armamentarium offers no unequivocally effective treatment. Nevertheless, correctly diagnosing dementia in its early stages may have considerable benefits for patients and family members. For example, patients are spared costly and inappropriate treatment related to misdiagnosis, and they and their families have time to prepare for the challenging financial, legal, and medical issues they will face. In addition, diagnosing dementia where it is not present causes distress and also may prevent identification and treatment of other conditions that are responsible for the patient's symptoms.

This *Clinical Practice Guideline* was developed to improve recognition of early-stage Alzheimer's disease and related dementias by encouraging initial assessment where warranted. Although differential diagnosis is beyond the scope of this guideline, it includes a list of resources for further clinical evaluation once probable dementia has been identified.

This guideline includes two important and useful clinical tools: (a) a table of symptoms that might indicate dementia, which should serve as triggers for an initial assessment, and (b) a sequence of steps to follow in conducting an initial assessment, which can be adapted according to the judgment of individual clinicians and the circumstances of individual patients. The guideline's principal audience is primary care clinicians. In addition, a wide range of other professionals who come in contact with older persons would benefit from awareness of behaviors that could signal the early stages of a dementing disorder.

A three-tier rating system indicates the relative strength of evidence supporting each recommendation. Recommendations strongly supported by data from the scientific literature are indicated by the letter A. The letter B denotes a statement with some scientific support that may be supplemented by expert panel opinion. The letter C is used when data from rigorous scientific studies are unavailable but an appropriate course of action is suggested by expert panel opinion, clinical experience, or both.

This guideline's key points include the following:

- Certain triggers should prompt a clinician to undertake an initial assessment for dementia rather than attribute apparent signs of decline to aging.
- An initial clinical assessment should combine information from a focused history and physical examination, an evaluation of mental and functional status, and reliable informant reports. It should also include assessment for delirium and depression.
- The Functional Activities Questionnaire, an informant-based measure, is particularly useful in the initial assessment for functional impairment.
- Among mental status tests, the Mini-Mental State Examination (MMSE), Blessed Information-Memory-Concentration Test, Blessed Orientation-Memory-Concentration Test, and the Short Test of Mental Status are largely equivalent in discriminative ability for early-stage dementia.
- Clinicians should assess and consider factors such as sensory impairment and physical disability in selection of mental and functional status tests and other confounding factors such as age, educational level, and cultural influences in interpretation of test results.
- When results of both mental and functional status tests are normal and there are no other clinical concerns, reassurance and reassessment in 6 to 12 months are appropriate. No standards are available for reassessment, but 6 to 12 months are suggested. If concerns persist, referral for a second opinion or further clinical evaluation should be considered (refer to resources listed in the guideline).
- When both mental and functional status tests yield findings of abnormality, further clinical evaluation should be conducted.
- When the initial assessment tests show mixed results (mental status impaired but no

functional losses, or vice versa), the patient should be referred for neuropsychological, neurological, or psychiatric evaluation, as indicated.
- The progressive nature of the cognitive impairment associated with early-stage dementia makes followup collaboration and continuity of care, for the patient, family, and caregivers, particularly important.

As research on dementia widens knowledge about genetic and other predisposing factors and produces new therapeutic approaches, early recognition and assessment of this devastating disorder will assume even greater importance.

1. Overview

Changes in some areas of cognitive function are associated with aging, but the majority of older persons remain active and productive until a very old age (Howieson, Holm, Kaye, et al., 1993). It is estimated that at least 2 million Americans suffer from a much more serious and debilitating form of mental decline termed "dementia." Dementia is a syndrome of progressive decline in multiple areas (or domains) of cognitive function, eventually leading to an inability to maintain occupational and social performance.

Early recognition and initial assessment of dementia was selected by the Agency for Health Care Policy and Research (AHCPR) as a subject for the development of a *Clinical Practice Guideline* for several reasons: the scope of the problem is significant, early-stage dementia is often misdiagnosed, costs associated with dementia are high, and early recognition of the condition has important benefits. Because the most prevalent dementing illness in the United States is Alzheimer's disease, it is used as a model for discussions in this guideline, unless otherwise noted.

Dementia in the adult population is a serious and growing medical, social, and economic problem (Cummings and Benson, 1992). The overall prevalence is estimated at 5 to 10 percent among persons ages 65 and older (Henderson and Huppert, 1984; Morris, 1994); the incidence increases with age and may peak in persons in their 70s or 80s. Recent estimates are that a minimum of 2 million persons in the United States -- and perhaps as many as 4 million -- suffer from cognitive decline attributable to dementia (Advisory Panel on Alzheimer's Disease, 1993; Evans, Scherr, Cook, et al., 1990). (Differences in estimates result from the different methods used by different investigators.)

Studies have documented health care providers' difficulties in correctly applying a diagnosis of dementia (O'Connor, Fertig, Grande, et al., 1993; Rubin, Glasser, and Werckle, 1987; Smith, Byrne, Arie, et al., 1992; Somerfield, Weisman, Ury, et al., 1991). In some instances, a diagnosis of dementia or Alzheimer's disease is applied when it is not present (Garcia, Reding, and Blass, 1981; Roca, Klein, Kirby, et al., 1984). Conversely, dementia is often unrecognized (Callahan, Hendrie, and Tierney, 1995; Hoffman, 1982; O'Connor, Pollitt, Hyde, et al., 1988; Williamson, Stokoe, Gray, et al., 1964). Underrecognition has been attributed to lack of attention to cognitive functioning in routine medical examinations (German, Shapiro, Skinner, et al., 1987; McCartney and Palmateer, 1985) and to misperceptions about the normal aging process. A tendency remains among some providers to consider mild dementing changes as "just old age" (Mant, Eyland, Pond, et al., 1988; Rubin, Glasser, and Werckle, 1987). Mild cognitive impairment, in particular, may be incorrectly viewed as an expected and inevitable part of growing older (Pinholt, Kroenke, Hanley, et al., 1987). Common myths about inevitable decline or impairment may contribute to these misperceptions. Indeed, some cognitive changes are associated with normal aging of the nervous system (e.g., slowing of information-processing speed). However, age-associated changes in function are benign and are neither progressive nor disabling. Dementia syndromes are disabling and should not be viewed as an inevitable part of growing older (Breitner and Welsh, 1995; Siegler, Poon, and Madden, 1995).

The costs of dementia to society are substantial. The economic burden includes not only the direct costs of medical and social services but also the indirect costs of dementia-related morbidity and mortality and lost productivity of those affected and their caregivers. Estimates of the overall cost burden of this condition range from $54 to $120 billion annually (Rice and Max, 1993). The noneconomic toll is incalculable.

The increase in research on normal and pathological aging permits an evidence-supported approach to identifying steps in early recognition and initial assessment of persons suspected of having Alzheimer's disease or a related dementia. Significant potential advantages may derive from early recognition and accurate identification of dementia. For example, in some cases the condition may be reversible; with appropriate treatment of some causes of dementia, symptoms may improve or be resolved. Early identification of dementia alerts affected persons and their families to potentially hazardous situations (White and Davis, 1990) and allows time to explore the services available for financial, legal, and medical care planning. As potential therapeutic modalities for dementias become available, early recognition and assessment of dementia will assume even greater importance (Lanska and Schoenberg, 1993).

Purpose and Scope

The purpose of this *Clinical Practice Guideline* is to assist health care providers in detection of Alzheimer's disease and related dementias in their early stages in selected persons. It is not intended to provide guidelines for differential diagnosis. Its fundamental premise is that there are "triggers" or clues that should prompt a clinician to undertake a preliminary assessment for early detection of a dementing illness. This approach relies on a combination of informant and patient reports and brief mental status assessments to identify a decline from previous levels of functioning. It also takes into account the influence of factors that can complicate interpretation of assessment results, such as concomitant impairments or physical or mental disabilities, and sociodemographic and cultural factors.

The guideline focuses on the first steps in early detection: identifying possible symptoms or triggers that might signal the presence of dementia; conducting an initial clinical assessment including assessing functional and mental status; and interpreting the results of this initial assessment to determine the need for further evaluation, such as neuropsychological, neurological, or psychiatric examinations. This guideline does not address specific components of a clinical evaluation and differential diagnosis of persons identified by the guideline as very likely to have dementia; Attachment Aprovides references to thorough approaches for further clinical evaluation.

After extensive review of the available evidence and discussion, the panel decided to make recommendations for early detection of dementia in persons in whom certain characteristics or triggers justify the effort of early detection, rather than recommend screening of entire segments of the population such as all those over some selected age. The decision not to recommend population-based screening was based on several factors, including the great variability in mental performance and general functioning among persons at every age and the presence of confounding variables such as level of education, ethnicity, and socioeconomic status. Currently available assessment tests lack adequate sensitivity and specificity for detection of early dementia in the general population. In the absence of other indications for assessment, their use as screening instruments could result in many diagnoses of dementia where it does not exist (false-positives) and many inappropriate reassurances of normality (false-negatives).

This guideline is intended for use by primary care clinicians. In different care settings, and when a multidisciplinary team is used, a nurse clinician or social worker might be the first person to see the patient. The health care professional functioning as the primary clinician is the principal target of this guideline. The guideline also will be useful to a wide range of professionals who are likely to come in contact with persons affected by dementia, including but not limited to psychologists, lawyers, and dentists. All professionals who work with older persons should be knowledgeable about the triggers or clues that might signal possible dementia. Most important, it is the judgment of this panel that there are triggers, as presented in Chapter 4, that should prompt a clinician to undertake the relatively simple evaluation described in this guideline for early detection of a dementing illness.

Methods for Guideline Development

AHCPR solicited nominations for an expert panel to develop this guideline through a *Federal Register* announcement and from professional and consumer organizations interested in the care of persons with Alzheimer's disease and related dementias. From a total of more than 150 nominations, AHCPR appointed 18 panel members, including 5 psychologists, 3 psychiatrists, 2 neurologists, 2 nurses, 1 internist, 2 geriatricians, 1 social worker, and 2 consumer representatives. The panel held three full meetings and several smaller panel group meetings beginning in June 1992.

The panel based its analytic approach on AHCPR principles for development of evidence-based clinical practice guidelines. Using these methods, the panel identified the clinical questions to be addressed in the guideline; developed systematic literature search strategies; reviewed, analyzed, and summarized the scientific evidence; and rated strength of evidence according to a three-level system (see subsection below entitled "Panel Recommendations and Strength of Evidence"). The panel then wrote guideline recommendations based on data from the scientific literature. Where scientific evidence was missing or inconclusive, panel consensus was used to support the guideline recommendation.

History of Guideline Focus

The panel was originally convened to develop a guideline entitled Screening for Alzheimer's and Related Dementias. During the first 18 months, the panel devoted considerable time to analyzing the literature on screening tests. The American Psychological Association (APA) conducted the primary literature search under contract to AHCPR; its work was then reviewed and a meta-analysis undertaken. On the basis of this analysis and after considerable deliberation, the panel reached three important conclusions: (a) of the most frequently used screening tests, no evidence existed that some should be recommended over others; (b) none of the tests had a high sensitivity for early or mild dementia; and (c) there was no evidence that a general screen for Alzheimer's disease or related dementias

would be efficacious, given the lack of unequivocally effective treatment and the difficulty of recognizing early dementia. These were valuable conclusions in themselves; however, they clearly dictated a redirection of the panel's work.

The panel concluded that the recognition of early dementia remained an important issue, for reasons previously stated, and changed the guideline focus to recognition and initial assessment of Alzheimer's disease and related dementias. The panel agreed to limit its scope to this subject and not to consider differential diagnosis. Work was assigned to panel subgroups whose members specialized in the topics delegated to them, and additional literature searches were conducted. Attachment B lists instruments for which specific literature searches were conducted.

Literature Search and Review

The primary and most extensive literature search, conducted by APA through January 1993, was undertaken to identify empirical studies of assessment of mental status instruments for differentiating between persons with and without dementia. A second search, from January through July 1993, was conducted to identify mental status instruments used in the assessment of persons with Alzheimer's disease. This literature was subjected to meta-analysis, as described below. The Guideline Technical Report for this guideline describes this process in greater detail. The panel conducted additional literature searches related to assessment of functional impairment to inform the development of the assessment flow chart, locate published material on risk factors for dementia, and identify relevant articles published after the date of the original searches. As a result of the peer review process, references unrelated to the meta-analyses were added through August 1995. This guideline includes a total of more than 300 references.

To assist the literature search and analysis on assessment instruments, the panel developed a list of key words or phrases (e.g., screening, assessment, cognitive, cognition, dementia, memory, neuropsychology), as well as criteria for selecting or rejecting abstracts or articles. The search process was guided by three criteria: (a) the tests should be sensitive to early or mild symptoms of dementia; (b) they should lend themselves for use in unselected populations, that is, be useful with a wide spectrum of persons with a number of comorbid conditions; and (c) they should have high clinical utility, that is, not require specialized equipment, extensive or complex procedures of scoring or administration, or extensive specialized training.

Eight inclusion criteria were identified for articles on assessment instruments. They should concern human studies, pertain to adult or elderly subjects, be written in English, assess memory complaints, be screening studies, be editorials or commentaries, be meta-analyses, and, finally, be evaluations of instrument effectiveness or discriminability. In addition, 24 criteria were used to exclude studies or records from the literature search process. If a record dealt with one or more of the following criteria, it was not selected: animal studies, children, non-English languages, etiology or pathology, biological markers, individual case studies, biochemistry, drug models, clinical trials, drug therapy, dexamethasone suppression, toxic encephalopathy, acquired immunodeficiency syndrome (AIDS), syphilis, neurosyphilis, multiple sclerosis, lumbar punctures, cerebrospinal fluid analysis, treatment, management, detection by neuroimaging, pathophysiology, physiological changes, and normal aging changes. The APA and the National Library of Medicine conducted comprehensive computerized literature searches of 20 electronic databases. These searches yielded a total of 8,198 records, which were entered into a Pro-Cite database. An additional 961 abstracts were contributed by panel members and other sources, for a total of 9,159 records.

Panelists then rated the abstracts or records in the database to identify those sufficiently promising to warrant obtaining copies of the full document. The ratings were guided by two broad criteria selected to identify the study as useful for the meta-analysis: (a) relevance to assessment of early detection of mild dementia (i.e., the study used a test, battery, interview, or technology that is at least conceivably useful for the assessment or screening of early or mild dementia) and (b) inclusion of quantitative information (i.e., the study is likely to contain empirical information on persons with dementia and a group of control subjects). On the basis of these criteria, panelists rated abstracts as 1, definitely retrieve; 2, retain citation but do not retrieve now; and 3, not needed, do not retrieve the reprint or retain the citation. The 671 abstracts with an average rating of 1.0 or 1.5 were retrieved and further evaluated.

The 671 articles were read and coded by panel project staff to obtain crucial information about the study design and findings that would be used for the meta-analytic evaluation. Only 178 of these 671 abstracts provided data relevant to the meta-analyses described below; 493 were rejected as unsuitable to provide data necessary for the meta-analysis. The two most frequent reasons for rejection were lack of control or dementia group (40 percent) and no suitable screening instrument (20 percent). Review of new studies yielded an additional 67 studies that were potentially suitable to provide data relevant to the meta-analyses. Of the 67 additional studies, 32 were judged suitable for meta-analysis.

Meta-Analysis

Meta-analysis is the method the panel chose for combining the scientific evidence on dementia assessment instruments. In meta-analysis, the index of an instrument's ability to discriminate between persons who do and do not have dementia is expressed in terms of a mean effect size, a statistic that summarizes the separation of average scores between the two groups in standard deviation units (Hedges and Okin, 1985). An average effect size is computed for each test. Higher effect sizes correspond to greater differences between the groups in average scores and thus greater discriminative ability (Hasselblad and Hedges, 1995). Further details of the meta-analysis are found in the *Guideline Technical Report.*

A total of 210 articles (178 from the original search and 32 of the new studies) were included in the meta-analysis (Hedges and Okin, 1985). The initial meta-analyses were conducted on a set of 100 tests or instruments, which included subtests or items from tests or mental status questionnaires. The effect sizes computed in these meta-analyses were calculated for control subjects versus patients with dementia that varied in stage or severity of disease. Studies of persons with severe-only or moderate-to-severe dementia had larger effect sizes than studies of persons with mild-only or mild-to-moderate dementia. The severity of dementia was the only between-study difference considered in the characterization of case patients and control subjects.

Table 1. Five-phase scheme for evaluation of mental status tests

Phase	Case patients	Control subjects	Purpose
Uncontrolled			
I	Narrow spectrum of disease		Performance of procedure
Case-Control			
II	Narrow typical	Healthy	Coarse distinctions
III	Expanded spectrum	Healthy	More subtle distinctions
IV	Inclusion of appropriate comorbidity	Inclusion of appropriate comorbidity	Clinical spectrum of pertinent challenges
Prospective			
V	Full specturm	Full spectrum	Cohort clinical trials

Source: Nierenberg AA, Feinstein AR. How to evaluate diagnostic marker tests. Lessons from the rise and fall of dexamethasone suppression test. JAMA 1988;259(11):1699-1702. Copyright 1988, American Medical Association. Used with permission.

But the panel came to realize that the failure to consider characteristics of the control subjects and the case patients could result in seriously misleading results concerning the efficacy of a psychometric instrument or mental status battery or test when applied under usual clinical conditions. Most studies in the literature that met the coding criteria for inclusion in the meta-analyses (see *Guideline Technical Report*) typically excluded patients with clinical conditions that might cause false-negative or false-positive results. As a consequence, such a test "can be used with confidence only to a narrow clinical spectrum that frequently does not include the patients for whom the test is most often ordered or needed" (Philbrick, Horwitz, and Feinstein, 1980). To identify mental status tests that would be clinically useful across a wide spectrum of persons, the panel adopted the five-phase evaluation scheme proposed by Nierenberg and Feinstein (1988), as shown in Table 1. Because Phase I does not involve a control or comparison group, Phase I studies were not relevant to the meta-analyses and thus were omitted from Attachment C, which presents a comparison of mental and functional status tests according to Phases II, III, and IV.

Healthy control subjects consisted of community volunteers or sometimes nonaffected spouses. Control subjects with comorbidity could include patients from primary care clinics, psychiatric clinic outpatients, memory or dementia clinic outpatients, or medical or surgical patients. Characteristics of case subjects were as follows: narrow spectrum of disease included moderate to severe Alzheimer's disease; expanded spectrum included mild or mixed Alzheimer's disease; and comorbidity among case subjects was most often depression, stroke, delirium, or other conditions that affected cognitive or functional performance.

Despite the voluminous literature on the subject, very few studies have been conducted on the most informative phases (i.e., IV or V). Thus, for Phase IV studies, only one instrument, the MMSE, had more than four contrasts; the remainder of the instruments had fewer than

four (most had only two contrasts). Consequently, two studies, each with a single contrast at Phase IV, represent extremely important if limited information.

Instruments for assessment of functional impairment were also subjected to meta-analysis. The 18 key instruments evaluated in the meta-analyses are listed in Attachment B. The results of the meta-analyses for selecting specific assessment instruments for mental and functional status are described in Chapter 4 (see also Attachment C).

Panel Recommendations and Strength of Evidence

After extensive review and analysis of the available scientific literature, the panel developed guideline recommendations supported by the evidence. Strength of evidence was rated based on the following criteria:

A
Strong Evidence. Evidence from studies that compare case patients who have dementia with control subjects who do not have dementia but do have comorbid or interfering conditions (most difficult level of discrimination).
B
Suggestive Evidence. The same type of evidence as in category A, but involving a smaller number of studies or a less consistent pattern of findings, or both.
C
Expert Opinion. Evidence from clinical experience described in the literature or derived from the consensus of panel members, or both. The panel's recommendations, strength-of-evidence ratings, and discussion of supporting evidence appear in Chapter 4.

Public Comment and Peer Review

A public meeting was announced in the *Federal Register* and held April 12, 1993, in Washington, DC. The purpose of this meeting was to give interested organizations, individuals, and agencies an opportunity to present written or oral testimony for the panel's consideration. The meeting elicited oral and additional written testimony from eight interested parties.

Later in the process of guideline development, drafts of the *Clinical Practice Guideline* were distributed for peer review. A second peer review was conducted for a subsequent draft that incorporated major revisions based on earlier review comments. Reviewers were selected from the following groups to represent a broad range of disciplines and clinical practice areas: health care professional and consumer organizations, participants in the public meeting, government agencies, and interested health care providers. A total of 109 reviewers submitted comments, which were collated and reviewed by the panel cochairs.

Recommendations for Further Research

In reviewing and analyzing relevant literature, the panel identified several areas related to the initial recognition of dementia that have not been investigated or have not been studied adequately. Areas identified for future research include the following:

- The relative costs of a simple approach to initial assessment of dementia versus much more expensive diagnostic procedures.
- The nature of depressive symptoms observed in early dementia, including evaluation of the effects of other coexisting chronic diseases. Several studies have noted an apparent decrease in the prevalence of depressive symptoms with increasing dementia, but questions remain about whether this reflects problems with current assessment methods or a real interaction between affective pathology and the severity of dementia.
- A prospective study to obtain valid estimates of the economic burden resulting from Alzheimer's disease and related dementias, including both direct and indirect costs.
- The incremental validity and reliability of functional status questionnaires that assess higher social and instrumental activities in the initial assessment of persons with dementia.
- Followup on suggestive new research, for example, on genetic aspects of dementia and written language as an early diagnostic clue to later development of Alzheimer's disease.
- Clinical implications of advances in early diagnosis of Alzheimer's disease and other dementias.
- Coding and standardization of database information to permit comparative studies.
- Caregivers in the community and support for patients, family members, and caregivers in dealing with behavioral and other problems.
- Health systems research, for example, health maintenance organizations and other systems, as more Americans become covered by alternatives to fee-for-service-based insurance systems.
- Legal and ethical considerations and protections related to dementia, especially if definitive early diagnosis becomes possible years before symptoms manifest.

In addition, the panel noted that other related research questions and topics under investigation will advance diagnosis and management of persons with dementia. Genetic screening for persons who may be at high risk for Alzheimer's disease, such as those with the apolipoprotein E 4 gene locus on chromosome 19, is a highly debated issue, particularly because currently no demonstrated intervention can prevent or delay the dementing process, and no evidence exists about predicting age of onset for persons with this genotype. Efforts to develop biological markers for the presence of Alzheimer's disease, such as tests that could be performed on samples of blood or cerebrospinal fluid, are important research topics for confirming a suspected diagnosis of Alzheimer's disease.

Public and Professional Education

Both the public and health care providers need education about early recognition of cognitive problems among older persons. Although the National Institute on Aging and the Alzheimer's Association are conducting educational efforts for both these groups (see Attachment D), additional education is needed. For patients and their families and caregivers, such information is vital in the effort to distinguish reversible causes of dementia from normal aging and other cognitive problems and to obtain suitable care. Education is also relevant for a wide variety of health care professionals and other service providers who may be in a position to notice the onset of memory and cognitive problems in older persons they see frequently. In an urban setting, this might be a bus driver; in a rural community, it might be a grain dealer. Bank tellers, pharmacists, grocery store clerks, neighbors -- all may become aware of cognitive changes in regular customers and friends.

In all cases, the purpose of educational activities is to increase the likelihood of early recognition and assessment of a potential dementing illness so that (a) concern can be eliminated if it is not warranted, (b) treatable conditions can be identified and addressed appropriately, and (c) nonreversible conditions can be diagnosed early enough to permit the family to plan for contingencies such as long-term care, and for the patient to participate as fully as possible in those decisions. For example, financial planning, supportive services, assistive devices, respite care, and use of appropriate service providers should be considered.

Educational programs related to dementia for the public and for health care providers should emphasize that symptoms of dementia are not a concomitant of normal aging and should not be ignored because of the mistaken belief that cognitive decline is an inevitable consequence of aging. Although changes in memory and cognition may accompany normal aging, significant impairment and disability are not a part of normal aging. In addition, the degree of concern felt by a person about memory problems and the severity of actual memory problems demonstrated during testing are not necessarily directly related (Cromwell, 1992).

Another important goal of educational programs related to dementia should be to clarify the difference between initial assessment and final diagnosis. A diagnosis or label such as Alzheimer's disease should not be applied prematurely.

Organization of the Guideline

This first chapter has described the purpose and scope of the guideline and the methods used by the expert panel to develop it. Chapter 2 includes background information on Alzheimer's disease and other dementias, such as major characteristics, prevalence and incidence, and costs associated with the condition. Chapter 3 addresses risk factors and causes of dementia. Chapter 4 presents specific guideline recommendations and summarizes supporting evidence. It includes a clinical algorithm for recognition and initial assessment and a table of symptoms that suggest possible dementia. Chapter 4also contains information about delirium and depression, which can account for or mask symptoms of dementia. The attachments contain information about specific mental and functional status tests and list additional resources that will assist health care professionals and caregivers.

Table 6. Symptoms that may indicate dementia

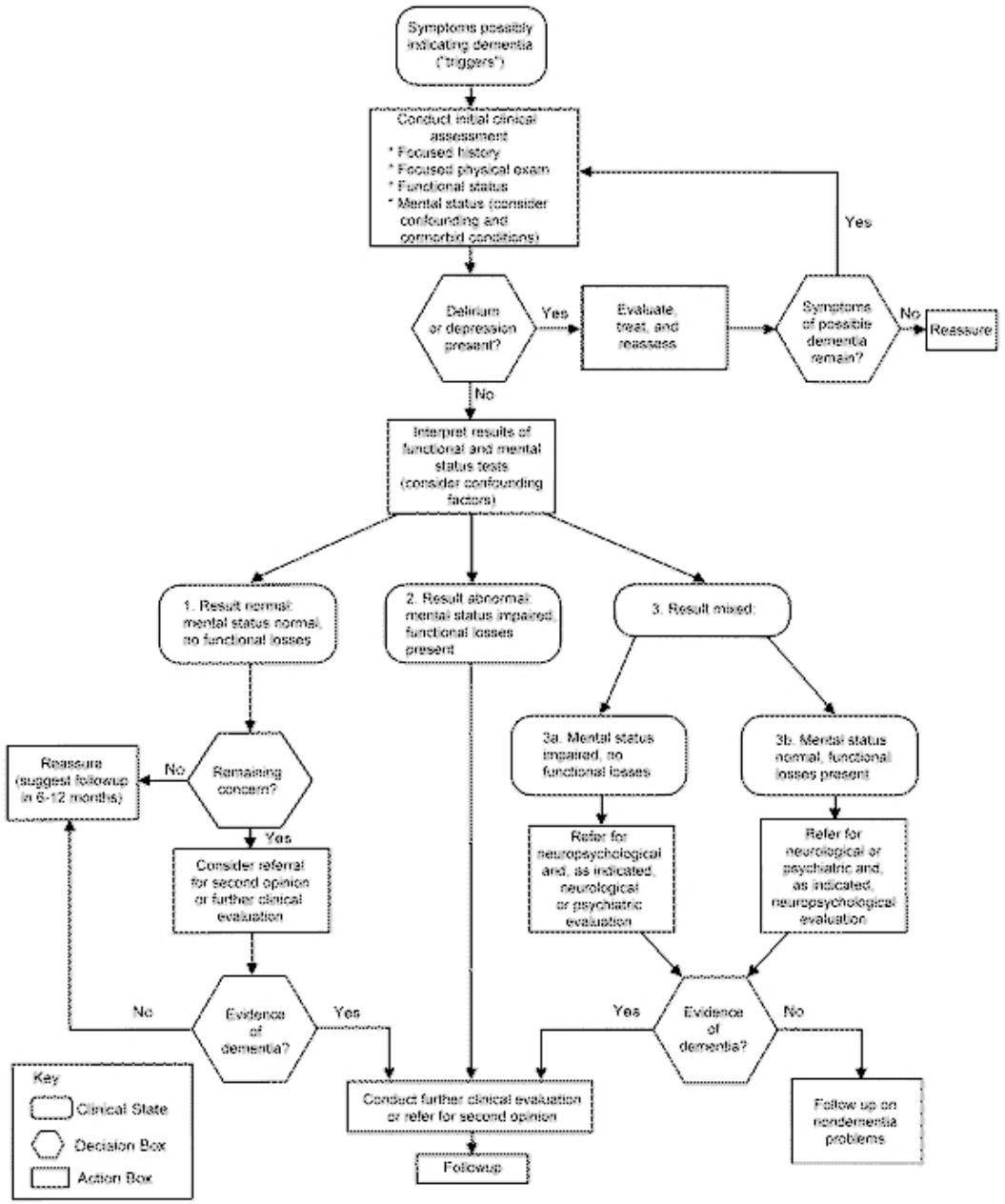

Figure: Flow chart for recognition and initial assessment of Alzheimer's disease and related dementias

Two key features of this guideline are designed as clinical aids in the early recognition of dementia. The list of symptoms of possible dementia (Table 6) helps clinicians and others identify patient behaviors that indicate the need for an initial clinical assessment. The flow chart (Figure) provides an efficient, step-by-step guide to the initial recognition and assessment of patients, as well as interpretation of initial test results.

2. Characteristics, Epidemiology, and Costs

Most people experience detectable changes in cognitive function as they age; however, these changes do not occur uniformly in all persons or at given ages (Schaie, 1990). Although health professionals, as well as patients and family members, often mistake the early symptoms of dementia for the normal deficits of aging, dementia has characteristics that distinguish it from normal aging and from other syndromes that involve cognitive problems. Because Alzheimer's disease is the most prevalent dementing illness in the United States, it

is used as a model for discussions in this guideline unless otherwise noted (Terry, Katzman, and Bick, 1994).

Table 2. Diagnostic criteria for dementia of the Alzheimer's (more...)

Dementia is an acquired syndrome in which progressive deterioration in global intellectual abilities is of such severity that it interferes with the person's customary occupational and social performance. Dementia is suspected when a person experiences a substantial decline in memory as well as other changes in cognition, personality, or both. Diagnostic criteria for dementia of the Alzheimer's type are listed in Table 2. Other presentations of dementia are possible, for example, with more prominent language dysfunction or behavioral or personality change. Dementia therefore differs from amnesia and aphasia, which are characterized by significant cognitive decline primarily in one major area, such as memory or language. In addition, patients with dementia retain a normal level of attention and consciousness until the late stage of the disease, which distinguishes dementia from delirium (see Chapter 4, section on assessing for delirium and depression).

Characteristics of Dementia

The changes characteristic of dementia fall into three general categories: cognitive, functional, and behavioral. Symptoms of deterioration in these domains are discussed below.

Cognitive Impairment

Cognitive manifestations may differ by type of dementia. Although memory problems are the most common cognitive deficits of dementia, a decline in other mental functions generally occurs. With Alzheimer's disease, for example, significant, objective, and progressive decline in other mental functions is a required component of the diagnosis.

Alzheimer's disease affects many aspects of cognition. For descriptive purposes, the changes that occur in the early stages of the disease can be divided into three groups: memory, language, and visuospatial dysfunctions (Storandt, Botwinick, Danziger, et al., 1984). It is important to note that these three areas of cognitive function also may be affected by age (as are attention, problem solving and abstraction, and general intelligence). The following discussion therefore contrasts normal aging with symptoms of possible early-stage dementia to help clinicians recognize the difference (see Chapter 4, section on triggers for recognition and initial assessment for the presence of dementia).

Memory. Memory is a complex function. For short-term or primary memory -- the ability to learn and briefly retain small amounts of information (i.e., for a few seconds or minutes, if not distracted) -- normal age-related changes are generally minimal. However, age may bring substantial changes in long-term or secondary memory, particularly the ability to learn large amounts of information and retain them after long delays. Declines in this type of memory become more frequent beginning around age 50 (Crook and West, 1990). Progressive deterioration of memory abilities is a hallmark of Alzheimer's disease. Persons with this disease, even in the earliest stages, have difficulty learning new information and retaining it more than momentarily (Duchek, Cheney, Ferraro, et al., 1991). An example is failure to remember a recent conversation. In the early stage of the disease, a person may be able to remember a phrase or telephone number long enough to repeat it but will lose the information if there is a delay (Welsh, Butters, Hughes, et al., 1991). Repeated conversations are a common result. As the disease progresses, new learning is severely curtailed, and "old" or remote memories also are gradually lost. Persons in the early stages of Alzheimer's disease have problems with the two aspects of information retrieval: prompted recall (e.g., recalling the U.S. President's name) and recognition (e.g., recognizing the President's name among others). Also severely affected, even in early stages, is personal episodic memory time-related information about oneself. An example is forgetting where one left a hairbrush after last using it. Recent research suggests that Alzheimer's disease affects some types of semantic memory or general knowledge (e.g., Mount Everest is the highest mountain in the world; see Nebes, 1989, for a review). An example is difficulty remembering names of common objects. In normal aging, semantic memory is usually well maintained; however, even in patients with Alzheimer's disease, aspects of general semantic knowledge are preserved, while distinctive features are affected (Nebes and Brody, 1988; Nebes, Norton, and Horn, 1984). Procedural memory (remembering how) does not appear to be affected by early-stage Alzheimer's disease to the same extent as declarative memory (remembering what). For example, although persons with Alzheimer's disease may have trouble remembering the name of their third-grade teacher, they are likely to remember the cursive writing skill learned from that teacher (LaBarge, Smith, Dick, et al., 1992). Some evidence suggests that persons with Alzheimer's disease of mild to moderate stage can retain new procedural learning of motor responses to relatively simple stimuli (Grafman, Weingartner, Newhouse, et al., 1990; Knopman, 1991).

Language. Language abilities are largely retained very well up to age 70. Those that decline over age 70 include word retrieval and word list generation. The ability to name an object when shown a picture of it (confrontation naming) declines in many older persons, as does

the ability to generate quickly a list of words that all belong to a common category or begin with a specific letter (word fluency) (Albert, Heller, and Milberg, 1988; Hultsch, Hertzog, Small, et al., 1992). Early in the course of Alzheimer's disease, some patients may have prominent language dysfunction (aphasia). Some studies suggest that aphasia is associated with more rapid deterioration (Kaszniak, Fox, Gandell, et al., 1978; Yesavage, Brooks, Taylor, et al., 1993). Several common language problems also may appear early in Alzheimer's disease (see Hart, 1988,for a review). An example is difficulty finding the desired words.

In early stages of the disease, persons usually maintain sentence structure (syntax) in expressive language, although it may become less complex (Heller, Dobbs, and Rule, 1992; Kemper, LaBarge, Ferraro, et al., 1993). The ability to pronounce single words and to write also remain intact until the disease becomes severe (LaBarge, Smith, Dick, et al., 1992; Nelson and O'Connell, 1978). Persons in the early stages of dementia do not appear to have much trouble with auditory comprehension, at least for short commands.

Visuospatial Abilities. Visuospatial abilities involve both production and recognition of three-dimensional or two-dimensional figures and objects. Compared with the young, many older persons show impairment in producing and recognizing three-dimensional drawings. For example, in a comparison of two groups of adults matched for visual acuity, one group with a mean age of 21 and one with a mean age of 67, the older persons were, on average, less accurate in drawing cubes or in discriminating among distorted and undistorted curves. There was considerable individual variability. The older persons were, however, equally able to copy a cube when given landmarks regarding the size of the lines (Plude, Milberg, and Cerella, 1986).

A possible variant of Alzheimer's disease involves more prominent early visuospatial dysfunction; becoming lost in a familiar neighborhood may be one of the first difficulties reported. Although some aspects of visuospatial difficulties may result from impaired memory (Henderson, Mack, and Williams, 1989), a subgroup of persons with Alzheimer's disease also may have neuropathologic lesions that affect the visual association cortex (Hof, Bouras, Constantinidis, et al., 1990). These lesions cause problems with complex visual functions such as figure-ground discrimination, visual recognition and synthesis, and spatial localization (Mendez, Mendez, Martin, et al., 1990) and make it difficult for the person to arrange objects at home.

Functional Impairment

A diagnosis of dementia requires impairment in functional competence, which includes social or occupational activities (see Table 2 for *Diagnostic and Statistical Manual of Mental Disorders,* 4th edition [DSM-IV] for diagnostic criteria for Alzheimer's disease [American Psychiatric Association, 1994]). Similarly, the National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's disease and Related Dementias Association (NINCDS-ADRDA) work group identified the assessment of functional performance as an important element of a comprehensive diagnostic evaluation for Alzheimer's disease (McKhann, Drachman, Folstein, et al., 1984).

In dementia, functional impairment is associated with two major types of abilities -- activities of daily living (ADLs) and instrumental activities of daily living (IADLs). ADLs are self-maintenance skills such as dressing, bathing, toileting, grooming, eating, and ambulating. IADLs are more complex, higher order skills such as managing finances, using the telephone, driving a car, taking medications, planning a meal, shopping, and working in an occupation. In Alzheimer's disease, problems typically appear in the conduct of IADLs and they progress to the inability to manage even less complex ADL functions of personal care (Reisberg, Ferris, and Franssen, 1985). Problems in performing the more complex IADLs may be the first indication of the disease to the patient or family.

Relationship Between Cognitive Impairment and Functional Performance. In the early stages of dementia, when the physician is attempting to make a first diagnosis, the patient may demonstrate different levels of cognitive and functional competence. Examples are driving without getting lost or taking medications without difficulty but then forgetting three-fourths of the items in a delayed-recall task. In more advanced stages of dementia, a clear relationship exists between the extent of cognitive impairment and functional performance (Bassett and Folstein, 1991; Heaton and Pendleton, 1981), although only a few studies have investigated the precise character of this relationship.

From cross-sectional research, Vitaliano, Breen, Albert, et al. (1984) reported that memory and attention deficits largely account for functional impairment in dementia patients. A followup study (Vitaliano, Russo, Breen, et al., 1986) showed that attention deficits predicted decline in functional performance for both ADLs and IADLs, even after the investigators controlled for initial levels of functioning. More recently, Henderson, Mack, and Williams (1989) found that visuoconstructive deficits documented by neuropsychological evaluation predicted spatial disorientation (wandering, getting lost, failing to recognize familiar environments), as reported by the caregivers of dementia patients.

Functional Assessment Instruments. Because dementia symptoms usually appear first in IADL tasks that reflect cognitive deficits (e.g., inappropriate dressing for occasion or

weather) rather than physical deficits, measurement of functional performance is warranted. Information on functional performance contributes importantly to the assessment of dementia, particularly the detection of mild forms of disease (Morris, McKeel, Storandt, et al., 1991). Assessment instruments that measure higher order social and instrumental activities are considered especially helpful when used in the context of a comprehensive evaluation for early dementia (Barberger-Gateau, Commenges, Gagnon, et al., 1992; Wilder, Gurland, Chen, et al., 1994).

Formal assessment of functional health emerged in the 1960s with the Index of Activities of Daily Living (Katz, Ford, Moskowitz, et al., 1963) and the Physical Self-Maintenance Scale (PSMS) and Lawton-Brody Instrumental Activities of Daily Living Scale (Lawton and Brody, 1969). More recently developed instruments include the Functional Activities Questionnaire (FAQ) (Pfeffer, Kurosaki, Harrah, et al., 1982) and the Structured Assessment of Independent Living Skills (SAILS) (Mahurin, DeBettignies, and Pirozzolo, 1991).

Implications of Functional Decline. Decline in functional abilities is one of the most troubling aspects of dementia for patients (Cotrell and Schulz, 1993) and their caregivers (Green, Mohs, Schmeidler, et al., 1993). Early in the dementing process, the loss of ability to function adequately may cause the patient to feel useless, dependent, and burdensome (Cotrell and Schulz, 1993). For families of persons with more advanced stages of dementia, the major problems of care include impairments of communication, eating and bathing, and wandering (Rabins, Mace, and Lucas, 1982). Incontinence is also a significant problem that causes stress for the patient and caregiver.

Caregivers have pragmatic concerns about the patient's ability to function independently, which include issues of safety, such as the ability to drive, follow medication directions, and use household appliances (e.g., remember to turn off an oven or stove burner). In addition to evaluating a patient's abilities in these areas, health care providers are often called upon to render judgments about functional competence (Loewenstein, 1990). Detailed information about the functional performance of persons with dementia is important for planning their care needs (Green, Mohs, Schmeidler, et al., 1993; Mahurin, DeBettignies, and Pirozzolo, 1991) and for legal and financial matters, including consent to treatment and competence to manage financial and other affairs. To structure care that is appropriate to each patient's current condition, it is important that functional performance be assessed with some regularity. Scheduled followup visits can help in this process of monitoring patients over time. Attachment D provides a list of national resources for patients, family members, and health care professionals to assist in some of these planning issues.

Behavioral Symptoms

Behavioral disturbances are prevalent in mild Alzheimer's disease (Rubin, Morris, Storandt, et al., 1987; Wild, Kaye, and Oken, 1994); other dementing disorders are also marked by a number of behavioral symptoms. These include personality changes, agitation, and symptoms of psychopathology such as mood disturbances, delusions, hallucinations, and misidentifications. Some of the behavioral disturbances such as agitation and psychotic symptoms usually are not found in early Alzheimer's disease but may be prominent in frontal lobe dementia syndromes. The physical changes in the brain that cause dementia evoke strong emotional responses, both in the patient and in those exposed to the condition. As the dementing disorder becomes evident in behavior changes, the patient and family members often experience considerable distress they may not be able to express. The patient may become frustrated by advancing debility; those who care for and about the patient are likely to be upset by signs of deterioration and behavior at odds with the person they know. The progressive nature of dementia over many years can create situations of unrelenting stress. Encouraging affected patients and families to talk about emotions they may not be able to identify can help them develop coping skills. It also may avert abusive situations that result when people react blindly to feelings they cannot express.

Additionally, when health care professionals are able to learn the personal characteristics that have defined and given meaning to patients' lives -- hobbies, professional accomplishments, family ties, expressions of faith-they can better understand and address patient and family frustrations as functional losses become evident. This knowledge informs decisions about patient care and helps clinicians respect the patient's wishes, even when he or she can no longer express preferences.

Like cognitive and functional deficits, behavioral disturbances vary considerably among patients. There is evidence that agitation, hallucinations, or delusions are associated with increased risk for nursing home placement (Steele, Rovner, Chase, et al., 1990) and may be associated with more rapid progression of cognitive impairment (Stern, Albert, Brandt, et al., 1994; Teri, McCurry, Edland, et al., 1995). Depression may be associated with increased mortality in patients with Alzheimer's disease (Burns, Lewis, Jacoby, et al., 1991).

In early or mild dementia, the most common behavioral symptoms include signs of depression and what can be considered broadly as personality changes (Rubin and Kinscherf, 1989; Rubin, Morris, Storandt, et al., 1987). Psychotic symptoms and clinically significant agitation seem to be fairly infrequent in early or mild dementia and seem to increase in frequency as the disease progresses to severe cognitive impairment (Reisberg, Franssen, Sclan, et al., 1989; Rubin and Kinscherf, 1989; Spector and Jackson, 1994). Reports are

less consistent for prevalence of depression as a function of disease severity, and available data vary depending on the assessment methods used and the nature of the depression being considered (Logie, Murphy, Brooks, et al., 1992; Wild, Kaye, and Oken, 1994).

Recent studies comparing levels of psychiatric symptoms in persons with vascular dementia and those with Alzheimer's disease have reported mixed findings (e.g., Cohen, Eisdorfer, Gorelick, et al., 1993; Corey-Bloom, Galasko, Hofstetter, et al., 1993; Sultzer, Levin, Mahler, et al., 1993). Distinguishing Alzheimer's dementia from vascular dementia is often very difficult. Many patients have both dementias, making the clinical diagnosis in such cases difficult if not impossible. In a sample of persons matched for severity of dementia, Sultzer and colleagues (1993) found that those with vascular dementia had more severe symptoms of depression, anxiety, and behavioral retardation (e.g., blunted affect, emotional withdrawal) than those with Alzheimer's disease. [In DSM-IV, nomenclature for "multi-infarct dementia" has been changed to "vascular dementia."] Cohen and colleagues (1993) found similar levels and patterns of psychiatric symptoms in persons with Alzheimer's disease and those with vascular dementia. However, persons with mixed Alzheimer's disease and vascular dementia had higher numbers of behavioral symptoms (e.g., wandering, abusiveness) than those with either Alzheimer's disease or vascular dementia alone.

Personality Changes. Although personality changes are among the most common behavioral problems in persons with dementia, they have been among the least intensively investigated. The available literature (e.g., Strauss, Pasupathi, and Chatterjee, 1993) suggests that assessing current and premorbid personality is feasible in persons with dementia. Data are inadequate, however, to estimate the sensitivity or the specificity of personality changes as a means of identifying persons with dementia. Family members often report that personality changes occur with Alzheimer's disease, but supporting data are retrospective in nature (Chatterjee, Strauss, Smyth, et al., 1992; Siegler, Welsh, Dawson, et al., 1991).

Rubin and colleagues (Rubin and Kinscherf, 1989; Rubin, Morris, and Berg, 1987) studied groups of persons with questionable and mild Alzheimer's disease and controls of similar age. They found that symptoms of passivity at times occurred by themselves, but agitation and self-centered behavior occurred most frequently in combination with symptoms of passivity. Rubin, Morris, and Berg (1987) evaluated these symptoms in this population as the disease progressed from early through moderate to severe dementia. For the respective severity levels, passive behavior increased in prevalence from 66 to 75 to 88 percent; agitated behaviors increased significantly from 30 to 46 to 67 percent; and self-centered behaviors increased from 34 to 58 to 63 percent.

Using an instrument designed for persons with head injury, Petry, Cummings, Hill, et al. (1988) compared spouses' ratings of personality changes in patients with Alzheimer's disease with changes related to retirement in control subjects. They reported that changes occurred regularly in the persons with Alzheimer's disease. These subjects were rated as having become more out of touch, more unreasonable, more lifeless, more unhappy, more irritable, less self-reliant, less mature, less enthusiastic, less stable, less affectionate, less kind, and less generous than before the onset of the disease. In contrast, there were no significant changes in control subjects. In the Alzheimer's disease group, only an increase in excitability was correlated with decreasing score on the Mini-Mental State Examination (MMSE). When the sample of persons with Alzheimer's disease was followed longitudinally, certain traits appeared to increase over time, such as listlessness, insensitivity, and coldness (Petry, Cummings, Hill, et al., 1989). Other traits increased and then plateaued, such as being out of touch, childish, reliant on others, unreasonable, lifeless, and uninterested in company.

Burns, Folstein, Brandt, et al. (1990) developed a scale to assess irritability, aggression, and apathy in persons with dementia. They reported that 58 percent of 31 persons with Alzheimer's disease were irritable, 32 percent were aggressive, and 48 percent were apathetic, with no relationship between symptomatology and score on the MMSE.

Both Siegler, Welsh, Dawson, et al. (1991) and Chatterjee, Strauss, Smyth, et al. (1992) investigated personality changes using relatives' ratings of patients on the NEO Personality Inventory (Costa and McCrae, 1989). Siegler and colleagues (1991), evaluating a series of persons with heterogeneous dementias or amnestic disorders, reported that they had become less conscientious, less extroverted, more neurotic, slightly less open, and more antagonistic. There was no correlation between these changes and MMSE scores. In a group of persons with Alzheimer's disease, Chatterjee and colleagues (1992) found a major decrease in conscientiousness followed by lesser increases in neuroticism and decreases in extroversion; changes in openness and agreeableness were smaller. Of these personality changes, only introversion was inversely associated with changes in MMSE scores; the other changes did not show a statistically significant association with the MMSE score.

Agitation. The most prevalent and the most intensively investigated behavioral disturbances in persons with dementia are states of agitation. Agitation poses a major clinical challenge in patients and in care settings such as nursing homes. Cohen-Mansfield, Marx, and Rosenthal (1990) investigated the phenomenology of dementia in nursing home residents; factor analysis suggested that agitation includes physically aggressive, physically nonaggressive (i.e., agitated behaviors, wandering), and verbally agitated behaviors. Although agitation

occurred in both cognitively intact and impaired nursing home residents, the symptoms differed. Cognitively intact residents exhibited primarily verbal agitation through symptoms that resembled exaggerations of coping mechanisms (e.g., complaining); those with dementia were more likely to show both physically nonaggressive and physically aggressive symptoms.

As reviewed by Deutch and Rovner (1991), reports on the frequency of agitation in persons with Alzheimer's disease from the community attending a dementia clinic varied from 24 to 48 percent; the frequency of physically nonaggressive behaviors was estimated at between 33 and 50 percent; physically aggressive behaviors, at approximately 30 percent; and verbally agitated behaviors, at 24 percent. The frequency of agitated behavior increases with the progression of Alzheimer's disease, with the highest rates in those with moderate or severe disease and a possible decrease in those with end-stage, extremely severe dementia (Reisberg, Franssen, Sclan, et al., 1989).

For caregivers at home, coping on a daily basis with agitation and other behavioral disturbances can engender mixed feelings, such as helplessness, distress, and anger toward the patient. Health care professionals can give family caregivers a valuable outlet for such emotions and acknowledge that they are natural responses to a highly stressful situation.

Symptoms of Psychopathology. Some behavioral symptoms have been more widely investigated, possibly because they are more obvious sources of disability, result in distress and danger to both affected persons and their caregivers, and are potentially treatable components of the dementia syndrome. These include mood disturbances and psychotic symptoms.

Mood Disturbances. Mood disturbances in dementia include both major depression and less severe but significant depressive states, such as depressive symptoms or "minor" depression, affective lability, and manic or hypomanic states (see Chapter 4 for a more extensive discussion of dementia and depression).

Wragg and Jeste (1989) summarized findings from 18 studies on depression in Alzheimer's disease. They reported that the frequencies of depressive symptoms ranged from 0 to 87 percent with a median of 41 percent and modal frequency between 40 and 50 percent. One study cited, Lazarus, Newton, Cohler, et al. (1987), comparing persons with Alzheimer's disease and control subjects, found a depression frequency of 40 percent in the Alzheimer's disease group and 12 percent in controls. Five studies reported a 19-percent median frequency of specific depressive disorders, primarily major depression, with most studies clustered between 10 and 20 percent. Additional studies reviewed by Burns (1991) do not alter these estimates.

Psychotic Symptoms. Wragg and Jeste (1989) also reviewed 21 studies of the prevalence of behavioral problems such as hallucinations and delusions in persons with Alzheimer's disease. The reported frequency of delusions at some time during the course of this illness ranges from 10 to 73 percent, with a median of 33.5 percent. Most reports show a frequency clustered between 30 and 38 percent. Reports on hallucinations range from 21 to 49 percent, with a median of 28 percent. Other symptoms such as misidentification of objects or people also are relatively common but have not been as intensively investigated. Although there is no clear consensus on the extent to which the prevalence of psychotic symptoms varies as a function of the stage of dementia or the degree of cognitive impairment, available data suggest that the frequency of psychotic symptoms at the earliest stages of the disease is low. Rubin and Kinscherf (1989), for example, report that delusions occurred in none of a group of control subjects without dementia, in 2 percent of those with questionable dementia, and in 21 percent of those with mild dementia. They report that hallucinations occur in 0, 0, and 13 percent, respectively; that misidentifications occur in 0, 0, and 12 percent; and that any psychotic symptoms occur in 0, 2, and 29 percent.

Prevalence, Incidence, and Survival

The panel conducted a second literature search on risk factors and epidemiology. It found that extensive surveys in various populations throughout the world report the rate of moderate-to-severe dementia as approximately 2 percent among persons ages 65 to 69; about 4 percent among those ages 70 to 74; 8 percent among those ages 75 to 79; and 16 percent among those ages 80 and older. These data show an overall prevalence of 5 to 10 percent among persons ages 65 and older (Henderson, 1990; Morris, 1994). When Evans, Funkenstein, Albert, et al. (1989) conducted a population survey of all older community-dwelling people in East Boston, with careful clinical assessments and identification of probable mild as well as more severe dementia, they found higher percentages: 10.3 percent of all persons age 65 and older, and 47.2 percent of those age 85 and older. The discrepancy between these data and others may be related to the diagnostic criteria of the Evans study, which were based on cognitive impairment only, with no requirement for functional impairment. Nevertheless, the Evans study does suggest that cognitive impairment may be more prevalent in the community than previously thought. Moreover, in a recent study of a multicultural community in north Manhattan (Gurland, Wilder, Cross, et al., 1995), high prevalence rates of dementia were found even when function was included in the diagnostic criteria.

Thus, it may be concluded that at least 2 million -- and possibly as many as 4 million -- residents of the United States are suffering from the cognitive decline of dementia (Advisory Panel on Alzheimer's Disease, 1993; Evans, Scherr, Cook, et al., 1990). These numbers are projected to rise to 7.5 to 14.3 million by the year 2040 (Evans, Scherr, Cook, et al., 1990).

Dementia has been reported to be more common among women (Breteler, Claus, van Duijn, et al., 1992), but this finding is probably attributable in part to the fact that women tend to live longer than men (Jorm, 1990). Evidence also suggests that dementia may be more common in community-living older black Americans (Heyman, Fillenbaum, Prosnitz, et al., 1991; Schoenberg, Anderson, and Haerer, 1985), perhaps because of this population's higher risk for vascular dementia. Gurland, Wilder, Cross, et al. (1995) compared large representative subgroups of elderly blacks, Latinos, and non-Latino whites. Non-Latino whites were found to have substantially lower rates of dementia (mainly Alzheimer's disease) than the other two groups, even when age was kept constant. However, ethnic and racial differences were considerably reduced when educational levels were made comparable.

Alzheimer's disease is the most common cause of dementia in the United States. It has been estimated that prevalence rates double every 4.5 years until at least age 90 (Jorm, 1990). In most Western European and North American countries, Alzheimer's disease accounts for 60 percent or more of dementing illnesses. A recent study from Sweden, however, found vascular dementia to be slightly more common than Alzheimer's disease (Skoog, Nilsson, Palmertz, et al., 1993). These differences could be related to variance in application of criteria across studies or different prevalence rates for underlying conditions such as hypertension or to differences in the relative educational levels of persons surveyed (see Age and Educational Levels section in Chapter 4).

Data on incidence of dementia are less extensive. An analysis based on the Framingham Heart Study found a doubling of incidence every 5 years beyond age 65, rising from 7 per 1,000 at ages 65 to 69 to 118 per 1,000 at ages 85 to 89 (Bachman, Wolf, Linn, et al., 1993). A recent longitudinal study of incidence found that either low educational level or low lifetime occupational attainment increased the risk of a diagnosis of dementia (Stern, Gurland, Tatemichi, et al., 1994). On the other hand, higher levels of education may either obscure detection of mild changes or provide some extra cognitive reserve capacity, delaying clinically evident onset.

Survival of dementia patients varies considerably. The literature is unclear about whether Alzheimer's disease significantly shortens the life span, except in early-onset cases. Persons with Alzheimer's disease typically live 8 to 10 years after onset, but the range is 1 to 20 years. Survival of persons with vascular dementia is usually shorter but is also highly variable. In Alzheimer's disease, typical causes of death are infections related to progressive debilitation, such as aspiration pneumonia, urinary tract infections, and sepsis from pressure ulcers.

Costs of Dementia

For affected families and society at large, dementia exacts a high economic toll in both direct and indirect costs. Direct costs include the dollars for diagnostic, treatment, and care services. Indirect costs are the expense of morbidity (the value of lost or reduced productivity of the patient and caregivers caused by illness) and mortality (the present value of future earnings lost because of premature death from disease). Although State and local governments and the Federal Government bear some of the cost of caring for persons with dementia, largely through Medicare and Medicaid, a substantial proportion of these costs is borne by families that provide unpaid care (Hu, Huang, and Cartwright, 1986; Rice, Fox, Max, et al., 1993).

According to the National Institute on Aging (1993), an estimated $90 billion is spent annually for Alzheimer's disease, including medical care, nursing home care, home care, and lost productivity. Others have developed different figures, depending on their approach to estimating indirect and direct costs.

Estimates of Direct Costs

To identify the direct costs of diagnosing, managing, and living with a health condition, one must know how many persons have the condition and the types, number, and costs of services provided. The number of persons with Alzheimer's disease is very difficult to determine. Estimates range from 1.35 million (Ernst and Hay, 1994) to 3.75 million (Evans, Scherr, Cook, et al., 1990). Other studies have yielded different estimates (Arenberg, 1990; Sapir, 1988). Estimates of prevalence of dementia vary among studies principally because of differences in diagnostic criteria and how they are implemented. Other reasons include whether they (a) are retrospective or prospective, (b) screen subjects or perform chart reviews, and (c) use test results alone or perform clinical assessments.

For a nationally representative study, the most efficient means of identifying cases is the diagnosis code of health care claims data; however, Alzheimer's disease, even when present,

is rarely coded in available databases. In a random sample of 5 percent of 1992 Medicare claims submitted for inpatient services (acute care, long-term care, skilled nursing facilities, rehabilitation hospitals, and psychiatric hospitals), only six cases among approximately 700,000 claims were identified with an ICD-9-CM (*International Classification of Diseases,* 9th revision, Clinical Modification) code of 331.0 (Alzheimer's disease) (Weis, 1992).

Alzheimer's disease is not coded for many reasons (Torian, Davidson, Fulop, et al., 1992), including the coding of other acute conditions as reasons for hospitalization (Congress of the United States, 1989). Without the means to identify cases reliably, one cannot use secondary databases to analyze the cost of diagnosing Alzheimer's disease. A prospective study is needed, and the cost of conducting a study that would provide reliable national estimates is great.

Costs of services are also difficult to determine. In addition to diagnosis, services needed by dementia patients and their families may include management, acute care, home- and community-based services, information and support for caregivers, respite care, legal and financial services, and nursing home care. The specific medical and long-term services that patients require are determined by factors such as stage and manifestations of disease and availability of caregivers in the home (Davis and Neuman, 1986).

Estimates of Total Costs

Either prevalence-based or incidence-based estimates are used to estimate the costs of illness. Prevalence-based estimates look at the direct and indirect economic burden incurred during a specific period of time (base period, often a year) as a result of the prevalence of a disease or illness. This includes the value of resources used or lost, regardless of time of onset of the disease. Incidence-based estimates, in aggregate, refer to the total lifetime costs of all cases of the disease or illness with onset in a given base year. Of the several studies that have attempted to estimate the indirect costs of informal care of Alzheimer's disease and other dementias (Hay and Ernst, 1987; Huang, Cartwright, and Hu, 1988; Rice, Fox, Max, et al., 1993), all but the Hay and Ernst study used the prevalence approach.

Rice and Max (1993) reviewed 19 studies of costs of aging-related diseases, converting the estimated costs of Alzheimer's disease and related dementias in those studies to 1991 dollars. When they converted data from the Hay and Ernst (1987) study (incidence data), total costs were $54 billion; the converted 1991 figure for costs from the Huang et al. (1988) study (prevalence data) totaled $120.8 billion. The substantial variation in estimated costs reflects the different approaches to cost estimation, methodologies, and sources of data.

The cost studies cited here attempt to capture the economic burden of dementia. Less quantifiable, but staggering, are the emotional and psychological costs dementia exacts from patients and their families. Along with the costs to society of Alzheimer's disease and other dementing conditions, it is important to acknowledge the profound nonfinancial toll, which may escalate over a period of many years.

3. Risk Factors and Causes of Dementia

Risk Factors

Despite the exponential increase in dementia associated with advancing age, the majority of persons are not affected even at very advanced ages. The incidence and prevalence rates for dementia may actually become level or decline beyond age 100 (Perls, 1995). Studies that examined potential genetic, environmental, infectious, and psychosocial risk factors for Alzheimer's disease found consistent evidence for only two other risk factors: family history of dementia and presence of Down syndrome (Amaducci, Falcini, and Lippi, 1992; Mortimer, 1994). Other proposed risk factors for which there is conflicting or insufficient evidence include previous head trauma, a family history of Down syndrome, thyroid disease, hearing loss, maternal age, and exposure to aluminum.

Family History of Dementia

Data from family studies vary by type of dementia and are complicated by confounding variables. Evidence suggests that by age 90, about one-half of the first-degree relatives of dementia patients develop dementia (Breitner, Silverman, Mohs, et al., 1988; Mohs, Breitner, Silverman, et al., 1987). In their reanalysis of 11 case-control studies, van Duijn, Clayton, Chandra, et al. (1991) reported an adjusted pooled odds ratio of 3.5 for family history. The risk is highest if a sibling was affected with Alzheimer's disease and increases with the number of first-degree relatives affected (Graves, White, Koepsell, et al., 1990).

Genetic studies based on the evidence from family histories show that genetic factors contribute to the development of Alzheimer's disease. Autosomal-dominant forms of the disease typically appear at young ages and are usually associated with early death. At least three autosomal-dominant forms of the disease, all with early-onset symptoms, have been

identified: a common one on chromosome 14 (Schellenberg, Bird, Wijsman, et al., 1992; Sherrington, Rogaev, Liang, et al., 1995) and rare ones on chromosome 1 (Levy-Lahad, Wijsman, Nemens, et al., 1995) and chromosome 21.

Recent studies suggest an association between alleles of the apolipoprotein E (apoE) gene locus on chromosome 19 and either increased risk for late-onset Alzheimer's disease (apoE 4) or protection against this risk (apoE 2 or 3) (Corder, Saunders, Risch, et al., 1994; Nathan, Bellosta, Sanan, et al., 1994; Poirier, Davignon, Bouthillier, et al., 1993; Roses, Strittmatter, Pericak-Vance, et al., 1994; Saunders, Schmader, Breitner, et al., 1993). Different studies have shown varying levels of association between the different apoE genotypes: 30 to 40 percent prevalence of Alzheimer's disease in persons with the homozygous apoE 4 genotype and as low as 15 to 20 percent prevalence in older persons who have either the apoE 2 or apoE 3 genotype.

It seems clear that other factors, such as other genes, life experiences, and environmental factors, must be involved to result in late-onset Alzheimer's disease. As Roses and colleagues (1994) suggest, it is not yet possible to depend on apoE genotyping for definitive guidance about diagnosis or treatment of Alzheimer's disease.

Presence of Down Syndrome

Most persons with Down syndrome develop the characteristic neuropathological brain lesions of Alzheimer's disease (i.e., neuritic plaques, granulovacuolar changes, cerebral vascular amyloidosis, Hirano bodies, and neurofibrillary tangles) by the age of 40 years (Wisniewski, Wisniewski, and Wen, 1985), although many do not demonstrate clinical features of dementia. According to Mortimer and Hutton (1985), almost all autopsies of persons with Down syndrome who have survived to at least 40 years of age reveal brain lesions typical of Alzheimer's disease. A recent study of apoE genotypes in persons with Down syndrome and in their first-degree relatives suggests that having the apoE 2 or 3 genotype may protect against what appeared to be an inevitable development of Alzheimer's disease, rather than the apoE 4 genotype being a causative factor (Hyman, West, Rebeck, et al., 1995; Royston, Mann, Pickering-Brown, et al., 1994). If this observation is confirmed, it could offer clues to the type of compound, analogous to apoE 2 or 3 gene products, that might prevent or delay the onset of Alzheimer's disease in susceptible persons.

Other Possible Risk Factors

There is evidence for a modest but significant association between Alzheimer's disease and earlier head trauma with loss of consciousness (Mortimer, van Duijn, Chandra, et al., 1991). This reported association may be explained by recall bias -- that is, overreporting by affected persons and underreporting by control subjects.

A low level of education is another suggested risk factor for dementia, but the evidence is mixed and suggests complex explanations. Although some studies find a strong association (Fratiglioni, Grut, Forsell, et al., 1991; Zhang, Katzman, Salmon, et al., 1990), other studies find none (Folstein, Bassett, Anthony, et al., 1991; Heyman, Fillenbaum, Prosnitz, et al., 1991). However, persons with limited formal education or occupational experience may be at higher risk for early detection (Amaducci, Falcini, and Lippi, 1992). They also may be at higher risk for false-positive diagnosis if a baseline evaluation is not available to demonstrate cognitive decline.

In summary, the only reasonably well-established risk factors for Alzheimer's disease are age, family history of dementia, and the presence of Down syndrome. Even though the incidence of Alzheimer's disease increases exponentially with age, it does not seem warranted to conclude that age alone is a risk factor that justifies steps to detect or rule out dementia.

Causes of Dementia

The term "reversible or potentially reversible" is used to distinguish a cognitive disorder that can be treated effectively to restore normal or nearly normal intellectual function from one that cannot ("nonreversible"). These terms are used instead of "treatable" and "nontreatable," because many of the nonreversible dementias such as Alzheimer's disease include symptoms that can be treated effectively (e.g., incontinence, wandering, depression).

Table 3. Causes of potentially reversible dementias (more...)

Table 4. Causes

These distinctions are somewhat arbitrary, however. For example, some cases of dementia attributable to hypothyroidism may reverse, whereas others may not. Factors in addition to the condition itself, such as duration of illness, severity of symptoms, and coexisting illness, can affect the reversibility of a condition with appropriate treatment (Barry and Moskowitz, 1988). For the purpose of this discussion, the classification of dementias as reversible or nonreversible will be that used in Tables 3 and 4 with the above

Table 4: Causes of nonreversible dementias

caveats noted.

Although many diseases are associated with both reversible and nonreversible dementias, a small number of disorders are responsible for a majority of dementia cases. Alzheimer's disease (see Table 2 for DSM-IV diagnostic criteria) is the most common dementing disorder in the United States. In a summary of nine clinical studies, Alzheimer's disease was responsible for about 66 percent of the total cases of dementia (Katzman and Rowe, 1992). Other progressive disorders, dementias, or both accounted for 17 percent of the cases and included vascular dementia, Parkinson's disease, Huntington's disease, progressive supranuclear palsy, amyotrophic lateral sclerosis, Creutzfeldt-Jakob disease, and dementia secondary to anoxia, trauma, and encephalitis. For approximately 11 percent of the cases, some specific therapy for the disease process was available, but the symptoms were not reversed. These included neurosyphilis, fungal infections, neoplasms, alcoholism, subdural hematoma, and hydrocephalus. About 5 percent of the cases in these series were classified as reversible dementias and included drug toxicity, metabolic changes, hepatic disease, hyponatremia, calcium disorders, deficiency of vitamin B_{12}, thyroid disease, and hypoglycemia.

A meta-analysis of 32 studies with a total of 2,889 subjects reflected similar findings (Clarfield, 1988). In these studies, the most common diagnoses among dementia patients were Alzheimer's disease (56.8 percent), vascular dementia (13.3 percent), depression (4.5 percent), alcoholic dementia (4.2 percent), and drug toxicity (1.5 percent). These findings are similar to those on frequency of dementing diseases reported by Wells (1977).

A summary of three neuropathologic series of dementia cases also found that Alzheimer's disease (about 45 percent) and vascular disease (15 percent) together accounted for more than half of all cases; mixed cases of both vascular and Alzheimer's disease accounted for less than 1 percent. Pick's disease accounted for 9 percent of the cases. Other diseases accounted for smaller percentages as follows: Parkinson's disease (1 percent), olivopontocerebellar atrophy (2 percent), alcoholic dementia (4 percent), hydrocephalus (6 percent), neoplasms (9 percent), Creutzfeldt-Jakob disease (3 percent), and inflammatory diseases, including neurosyphilis (6 percent) (Katzman and Rowe, 1992). Because of the small number of autopsies done, there is considerable potential for bias.

Reversible Dementias

Many disorders resulting in dementia are partially or completely reversible (see Table 3), but in most studies these disorders account for less than 20 percent of patients with dementia (Arnold and Kumar, 1993; Erkinjuntti, Wikström, Palo, et al., 1986; Larson, Reifler, Featherstone, et al., 1984; Larson, Reifler, Sumi, et al., 1985; McIntyre and Frank, 1987; Rabins, 1988; Smith and Kiloh, 1981). For further detail, see Clarfield (1988) and Small and Jarvik (1982).

Despite the relatively modest percentages represented by reversible causes of dementia, as well as treatable aspects of nonreversible dementias, it is important to recognize them. The potential to reverse the condition or halt or delay deterioration is among the most compelling justifications for early recognition of a dementing disorder. Knowledge of the patient and alertness to changes suggesting dementia can trigger timely actions or referrals that enhance quality of life and, in the case of delirium, even save lives.

As noted, among the most frequent reversible causes of dementia are depression (depressive pseudodementia), alcohol abuse, and drug toxicity. Katzman, Lasker, and Bernstein (1988) reviewed diagnoses in nine published series of clinical cases and found that drug toxicity was the most common cause of reversible dementia (2.7 percent of all cases). Other causes of dementia, such as normal-pressure hydrocephalus, neoplasms, metabolic disorders, trauma, and infection, occurred less often.

Few studies of potentially reversible dementia have provided followup of identified cases to determine if the patients improved with treatment. Of the 32 studies analyzed by Clarfield (1988), 11 had followup. In the approximately 13 percent of patients with potentially reversible causes of dementia, only 11 percent actually improved with treatment, and only 3 percent had complete reversal.

Alcohol. Of the several toxins that can produce dementia, alcohol is associated with the highest frequency of dementia. The increasing incidence of alcoholism in older persons makes this an important consideration. Prolonged, heavy ingestion of alcohol may result in an amnestic disorder with cognitive deficits limited to memory impairment that is not a classic dementia by DSM-IV criteria (American Psychiatric Association, 1994; Brust, 1993; O'Brien, 1994; Victor, Adams, and Collins, 1989). This disorder, Wernicke-Korsakoff syndrome, is generally attributed to associated thiamine deficiency. Alcohol amnestic syndrome often follows an acute episode of Wernicke's encephalopathy; if the Wernicke's encephalopathy is treated early, alcohol amnestic syndrome could be prevented. Once this syndrome is established, there is generally only slight improvement over time.

A dementia that does meet DSM-IV criteria, alcohol-induced persisting dementia, has also been associated with prolonged, heavy ingestion of alcohol (American Psychiatric Association, 1994; Brust, 1993; O'Brien, 1994). This dementia persists after alcohol intake

has stopped, and the etiologic role of alcohol in this disorder is controversial. Other nutritional disorders, such as multiple vitamin, protein, and calorie deficiencies, occur commonly in chronic alcoholics and have been linked to cognitive impairment. Correcting these deficiencies may improve cognitive function to some extent.

Table 5. Some medications that may cause cognitive impairment[a]

Type of medication	Generic name	Common trade name(s)
Anticholinergic agents	scopolamine	Transderm Scop, Isopto-Hyoscine
	orphenadrine	Norflex, Norgesic[b], Norgesic Forte[b]
	atropine	various, Lomotil[c]
	trihexyphenidyl	Artane
	benztropine	Cogentin
	meclizine	Antivert, Bonine
	homatropine	Isopto-Homatropine, Hycodan[c]
Antidepressants	amitriptyline	Elavil, Endep, Etrafon[c], Triavil[c], Limbitrol[c]
	imipramine	Tofranil
	desipramine	Norpramin
	doxepin	Sinequan
	trazodone	Desyrel
	fluoxetine	Prozac
Antimanic agents	lithium	Eskalith, Lithobid, Lithotabs
Antipsychotic (neuroleptic) agents	thioridazine	Mellaril
	chlorpromazine	Thorazine
	fluphenazine	Prolixin
	prochlorperazine	Compazine
	trifluperazine	Stelazine
	perphenazine	Trilafon, Etrafon[c], Triavil[c]
	haloperidol	Haldol
Antiarrhythmic agents (oral)	quinidine	Quinidex, Quinaglute
	disopyramide	Norpace
	tocainide	Tonocard
Antifungal agents	amphotericin B	Fungizone
	ketoconazole	Nizoral
Sedative/hypnotic agents		
Benzodiazepine derivatives	diazepam	Valium, Valrelease
	chlordiazepoxide	Librium, Libritabs, Librax[c]
	lorazepam	Ativan
	oxazepam	Serax

	flurazepam	Dalmane
	triazolam	Halcion
	alprazolam	Xanax
Barbiturate acid derivatives	phenobarbital	various, Donnatal[c]
	butabarbital	Butisol
	butalbital	Fiorinal[b] [c], Fioricet[c], Esgic[c]
	pentobarbital	Nembutal
Chloral & carbamate derivatives	chloral hydrate	Noctec, Aquachloral
	meprobamate	Miltown, Equanil, Equagesic[b]
Antihypertensive agents		
Beta adrenergic antagonists	propranolol	Inderal, Inderide[c]
	metoprolol	Lopressor
	atenolol	Tenormin
	timolol	Timoptic
Alpha-2 agonists	methyldopa	Aldomet, Aldoril[c]
	clonidine	Catapres, Catapres-TTS, Combipres[c]
Alpha-1 antagonists	prazosin	Minipress
Calcium channel blockers	verapamil	Calan, Isoptin
	nifedipine	Procardia, Adalat
	diltiazem	Cardizem, Cardizem CD
Inotropic (cardiotonic) agents	digoxin	Lanoxin, Lanoxicaps
Corticosteroids	hydrocortisone	Cortef, Cortisporin[c], Neo-Cortef[c], Cortaid
prednisone	Deltasone, Prednisone Intensol	
methylprednisone	Medrol, Solu-Medrol	
dexamethasone	Decadron, Neo-decadron[c]	
Nonsteroidal anti-inflammatory agents	ibuprofen	Motrin, Rufen, Advil, Nuprin, Medipren
	naproxen	Naprosyn, Anaprox, Aleve
	indomethacin	Indocin
	sulindac	Clinoril
	diflunisal	Dolobid

	choline magnesium trisalicylate	Trilisate, Tricosal
	aspirin	various
Narcotic analgesics	codeine	Tylenol with Codeine[c], Robitussin AC[c], Brontex[c], other codeine cough preparations
	hydrocodone	Lortab[c], Lorcet[c], Vicodin[c], Hycodan[c], Hycomine[c], Tussionex[c]
	oxycodone	Percodan[b], Percocet[c], Tylox[c], Roxicet[c]
	meperidine	Demerol, Mepergan[c]
	propoxyphene	Darvon, Darvon-N, Darvocet-N[c], Wygesic[c], Darvon Compound[b]
Antibiotics	metronidazole	Flagyl, Metrogel
	ciprofloxacin	Cipro
	norfloxacin	Noroxin
	ofloxacin	Floxin
	cefuroxime	Zinacef, Ceftin
	cephalexin	Keflex
	cephalothin	Keflin
Radiocontrast media	metrizamide	Amipaque
	iothalamate	Conray
	diatrizoate	Hypaque, Renovist
	iohexol	Omnipaque
H[2] receptor antagonists	cimetidine	Tagamet, Tagamet HD
	ranitidine	Zantac
	famotidine	Pepcid
	nizatidine	Axid
Immunosuppressive agents	cyclosporine	Sandimmune
	interferon	Intron A, Roferon A, Actimmune
Antineoplastic agents	chlorambucil	Leukeran
	cytarabine	Cytosar-U
	interleukin-2	
	spirohydantoin mustard	Spiromustine
Anticonvulsants	phenytoin	Dilantin
	valproic acid	Depakene, Depakote
	carbamazepine	Tegretol
Anti-Parkinsonian agents (see also anticholinergic agents)	levodopa levodopa/carbidopa bromocryptine	Larodopa Sinemet Parlodel Permax

agents)	pergolide	
Antiemetics	prochlorperazine	Compazine
	metoclopramide	Reglan
	hydroxyzine	Atarax, Vistaril
	promethazine	Phenergan
	trimethobenzamide	Tigan
	diphenhydramine	Benadryl, Dramamine
	meclazine	Antivert
Skeletal muscle relaxants	cyclobenzaprine	Flexaril
	methocarbimol	Robaxin
	carisoprodol	Soma, Soma Compound[b]
	baclofen	Lioresal
	chlorzoxazone	Parafon Forte, Paraflex
Antihistamines/decongestants	diphenhydramine	Benadryl, Tylenol PM[c], Sominex, other OTC cough/cold preparations
	chlorpheniramine	Chlor-Trimeton, Deconamine[c], Contac[c], Tylenol Cold[c], Hycomine[c], other OTC cough/cold preparations[c]
	brompheniramine	Dimetane, Dimetapp[c], Drixoral[c], other OTC cough/cold preparations[c]
	pseudoephedrine	Sudafed[c], Actifed[c], Robitussin PE[c], Dimetapp[c], Entex[c], Drixoral[c], Tylenol Cold[c], Claritin-D[c], other OTC cough/cold preparations[c]
	phenylpropanolamine	Ornade[c], Triaminic[c], Poly-Histine[c], Hycomine[c], other OTC suppressant preparations[c]

[a] These are examples only; new medications appear regularly.
[b] These compounds contain aspirin.
[c] These compounds may contain other active ingredients.
Source: Guideline panel.

Drugs. Drug use, particularly drug interaction resulting from polypharmacy (the administration of many drugs together), is a common cause of cognitive decline in elderly persons. Physicians often prescribe agents such as antidepressants, antiarrhythmics, antihypertensives, analgesics, and derivatives of digitalis simultaneously, without attention to their effects on cognition. For some of these drugs, the effects can be additive or synergistic. Moreover, frequent use of hypnotic medication for sleep in elderly persons can lead to a constant state of confusion or delirium. Withdrawal of centrally acting agents, particularly antidepressants, hypnotics, and analgesics, can improve cognitive function significantly. Table 5 lists some medications that can result in cognitive change (for reviews, see Abranowicz, 1986; Caird and Scott, 1986; Larson, Kukull, Buchner, et al., 1987; Morrison and Katz, 1989). Clinical experience also suggests that in older persons the "short-acting" psychotropic agents have longer-lasting effects. Clinicians should be alert to the signs of drug interactions. They can encourage the patient and family members or caregivers to keep a complete record of all the patient's medications, dosages, and schedules of administration, and to bring that record with them on each visit to a health care provider. A reminder that, for the purposes of recordkeeping, "medications" includes nonprescription products such as aspirin can be helpful. Patients may not know that most pharmacies will be pleased to keep a computerized record of medications prescribed by all

their physicians.

Psychiatric Disorders. Clinically significant numbers of patients who present with apparent dementia have a major psychiatric disorder that accounts for their cognitive problems. Estimates range from 1 to 31 percent of persons diagnosed with progressive dementing illness (Katzman, Lasker, and Bernstein, 1988). Depression is often misdiagnosed as dementia and vice versa (see the section in Chapter 4, Assessing for Delirium and Depression). The AHCPR-sponsored guideline, *Depression in Primary Care: Volume 1. Detection and Diagnosis*, offers a detailed discussion of diagnosis and treatment of depression (Rush, Golden, Hall, et al., 1993). Other psychiatric conditions that sometimes present with or mimic manifestations of dementia include schizophrenia (especially the paranoid form), bipolar disorders, and severe personality disorders. Given the frequency of a dementia misdiagnosis involving a psychiatric problem, followup monitoring and continuity of care are especially valuable in ensuring that the patient has been correctly diagnosed and is receiving suitable treatment. Indeed, the fact that psychiatric disorders can mimic dementia is one reason for undertaking the steps involved in initial assessment of an apparent dementing disorder.

Normal-Pressure Hydrocephalus. This is a disorder in which an abnormal accumulation of fluid in the cerebral ventricles compresses the brain. It is important as a diagnostic consideration because it is one of the causes of potentially reversible dementia (Arnold and Kumar, 1993). Although normal-pressure hydrocephalus is generally reported to account for less than 2 percent of all cases of dementia, some series indicate that it accounts for up to 6 percent of all cases (Katzman and Rowe, 1992; Wells, 1977). It occurs in middle-aged and older persons and is associated with dementia consisting of memory loss, confusion, slowness to respond, and paucity of thought that occurs over the course of weeks to years. Gait apraxia and urinary incontinence are also usually present. Although the condition may result from subarachnoid hemorrhage, trauma, or meningeal infection, most patients have no known precipitating illness or event.

Nonreversible Dementias

Alzheimer's disease and a small number of other disorders cause most cases of nonreversible dementia. More inclusive discussions of nonreversible dementias are available in articles by Katzman and Rowe (1992); Katzman, Terry, and Bick (1978); Khachaturian (1985); O'Brien (1994); Small and Jarvik (1982); Whitehouse (1993); and Wurtman, Corkin, Growdon, et al. (1990). Nonreversible disorders aside from Alzheimer's disease (see Table 2 for DSM-IV diagnostic criteria) are discussed below. Other relatively rare conditions also have nonreversible dementia as a feature (see Table 4).

Vascular Dementia. Vascular dementia, generally cited as the second most common of the nonreversible dementias, results from loss of neuronal tissue through death of brain tissue caused by interruption of blood supply, for example, by atherosclerotic lesions or from emboli. Hypertension with resultant cerebral infarctions is the most important, recognized, and preventable risk factor for vascular dementia; emboli from the heart or elsewhere within the vascular system are other causes. Vascular dementia frequently presents with a stepwise progression of symptoms, each with an abrupt onset, often in association with a neurologic incident. Focal neurologic findings, changes in tone and reflexes, and pseudobulbar palsy are common features of the illness. Vascular dementia is generally classified as a nonreversible dementia; however, appropriate treatment of hypertension and other risk factors for cerebrovascular disease is critical for prevention of further damage.

Pick's Disease. Pick's disease is a neurodegenerative disease characterized by severe cortical atrophy, most prominently of the frontal and temporal lobes. Persons with Pick's disease commonly show early signs of severe frontal lobe or temporal lobe dysfunction, characterized by general decline in mental function, changes in behavior patterns, and lack of insight. Later, loss of retentive memory, loss of language functions, and prominent grasp and sucking reflexes may occur. The disease is relentlessly progressive, generally over the course of 2 to 7 years, with the later stages characterized by features attributable to damage of the basal ganglia. The condition is usually sporadic but can occur in families.

Parkinson's Disease. Parkinson's disease is a progressive neurodegenerative disorder characterized by rigidity, bradykinesia, tremor, and postural instability resulting in disturbances of speech, gait, and coordination. Dementia associated with Parkinson's disease is insidious in onset and heralded by disorientation at night; its etiology has not been determined (Cedarbaum and Gancher, 1992; Yahr and Bergmann, 1986). Some cognitive impairment occurs in a large percentage of persons with Parkinson's disease; estimates range from 22 to 40 percent (Celesia and Wanamaker, 1972; Sroka, Elizan, Yahr, et al., 1981). Overall, Parkinson's disease accounted for about 1 percent of all instances of dementia in the studies analyzed by Clarfield (1988) and in the neuropathologic series of Katzman and Rowe (1992).

AIDS-Related Dementia. Although AIDS-related dementia (also referred to as "AIDS-related complex") is uncommon in older persons, it warrants diagnostic consideration for patients with a suspected history of risk factors or behaviors, such as pre-1985 transfusions, history of unprotected sex, and injection drug use. As described in the DSM-IV (American Psychiatric Association, 1994), where it is called "dementia due to HIV disease," AIDS-

related dementia is characterized by forgetfulness, slowness, poor concentration, and difficulties with problem solving. Prominent behavioral symptoms include apathy and social withdrawal. Physical examination may reveal tremor, impaired rapid repetitive movements, imbalance, ataxia, hypertonia, generalized hyperreflexia, positive frontal release signs, and impaired pursuit and saccadic eye movements (Arendt, Hefter, Neuen-Jacob, et al., 1993; Kaeming and Kaszniak, 1989). Although not designed to address AIDS-related dementia, the algorithm for initial assessment presented in the Figurein Chapter 4 might be considered during diagnosis, particularly for patients at high risk.

Knowledge of the risk factors and causes of dementing disorders, particularly the most common forms, is a valuable tool in the conduct of an initial assessment for suspected dementia, as described in the next chapter.

4. Recommendations for Recognition and Initial Assessment of Dementia

The panel recommendations, strength-of-evidence ratings, and discussion of supportive evidence are presented in this chapter. Criteria for the strength-of-evidence ratings are explained below.

A
Strong Evidence. Evidence from studies that compare case patients who have dementia with control subjects who do not have dementia but do have comorbid or interfering conditions (most difficult level of discrimination).
B
Suggestive Evidence. The same type of evidence as in category A but involving a smaller number of studies, or a less consistent pattern of findings, or both.
C
Expert Opinion. Evidence from clinical experience described in the literature, or derived from the consensus of panel members, or both.

Triggers for Recognition and Initial Assessment for the Presence of Dementia

Any concerns about cognitive decline or function expressed by the patient, family, or others or observations by the health care professional working directly with the patient should trigger an initial assessment for dementia.

> The symptoms possibly indicating dementia listed in Table 6provide clues to the health care provider for recognition and initial assessment of dementia. (Strength of Evidence = C)

Any positive response to the items listed in Table 6 generally warrants initiation of an assessment for the presence of dementia or other related conditions, as shown in the Figure. A number of factors might trigger examination for possible dementia; examples are included in Table 6. Concerns about these symptoms can be brought to the clinician's attention by the patient, family members, or others. In addition, clinicians who are following an older patient should be vigilant for signs of cognitive changes during followup office visits (see Table 6). For example, they should look for failure to arrive at the right time for appointments, difficulty discussing current events in an area of interest, word-finding difficulties, and changes in behavior or dress.

Table 6 is a clinical guide, not a validated assessment instrument. It is similar to the recent Alzheimer's Association (1995) lay publication,*Is it Alzheimer's? Warning Signs You Should Know*. It was developed by the panel from clinical experience and the dementia literature to allow clinicians to focus quickly on those areas of concern where further questioning will be most productive.

The clinician's awareness of the patient's current condition, history, and social situation (living arrangements, degree of support services, isolation) must guide the decision to initiate an assessment for dementia in asymptomatic persons who have possible risk factors. No studies support or refute the value of assessing for dementia based on the presence or absence of any combination of risk factors in asymptomatic persons. Thus, even though increasing age is associated with increasing risk, there is no evidence for the benefit of assessing all asymptomatic older persons for dementia. However, some clinicians may decide to assess cognition, for example, in an adult patient with Down syndrome, to detect early changes in cognitive function or to provide a baseline against which later cognitive assessment can be evaluated. As another example, certain groups of older persons, such as those who live alone and those who are socially isolated, might be at special risk for missed or ignored symptoms of early dementing changes in cognitive performance and function.

This, in turn, places these persons at risk for various harmful consequences (e.g., poor nutrition might result from memory loss and failure to eat properly and might contribute to weakening of the immune system; reduction in the ability to concentrate might lead to unsafe driving behaviors in persons who drive an automobile).

Initiating an Assessment for Alzheimer's Disease and Related Dementias

Determining the presence of a dementia syndrome is challenging. Identifying mild cases of dementia can be difficult (Berg, 1990; Lanska and Schoenberg, 1993) and requires consideration of complex data from careful clinical assessment, as well as from informant reports whenever available (O'Connor, Pollitt, Hyde, et al., 1991).

In accordance with the current criteria for the diagnosis of dementia (DSM-IV; American Psychiatric Association, 1994) (see Table 2), evidence for decline from previous levels of functioning and for impairment in multiple cognitive domains is required before concluding that dementia has been identified and before further clinical evaluation to determine etiology is undertaken. Dementia, or acquired cognitive impairment, must be distinguished from cases of lifelong cognitive impairment and from cognitive impairment with clouding of consciousness (delirium).

> An initial clinical assessment that combines multiple and varied sources of information is recommended to evaluate patients with suspected dementia. (Strength of Evidence = B)

The recommended assessment process is represented in the Figure (Flow Chart for Recognition and Initial Assessment of Alzheimer's Disease and Related Dementias, developed by the panel) and in the corresponding text. The flow chart was designed as a general guide to initial recognition and assessment of dementia. It is not intended as a set of strict decision rules but rather as a guiding framework to be used in conjunction with clinical judgment.

Interpretation of clinical and quantitative assessment data is complicated by several factors, including the patient's age, premorbid intelligence, education level, cultural background, psychiatric illness, sensory deficits, and comorbid conditions. Thus, clinicians are cautioned to consider these factors when applying the assessment framework in specific patient situations.

Once the symptoms of possible dementia in Table 6 have been recognized and clinical judgment indicates, an initial clinical assessment should be conducted. This initial assessment consists of several important components, including a focused history, a focused physical examination, and assessments of functional and mental status.

Focused History

> A focused history is critical in the assessment of dementia. The history should include relevant medical, family, social, cultural, and medication history (including alcohol use), as well as a detailed description of the chief complaint. (Strength of Evidence = C)

A focused history must identify any signs and symptoms listed in Table 6 and document the chronology of the problems. Of particular importance are the mode of onset (abrupt versus gradual), the progression (stepwise versus continuous decline; worsening versus fluctuating versus improving), and the duration of symptoms, although these are often difficult to assess with certainty.

The medical history should include inquiries about relevant systemic diseases, psychiatric disorders, and known neurological disorders, including history of head trauma. It also should include any history of alcohol or substance abuse and exposure to environmental toxins. Because a variety of medical conditions can cause or contribute to cognitive impairment, a careful review is indicated of any intercurrent, infectious, or metabolic illness, such as pneumonia, urinary tract infection, diabetes, or acute or chronic renal failure.

A thorough family history can contribute importantly to the initial evaluation for dementia. A family history of early-onset Alzheimer's disease or other rare genetic conditions leading to dementia such as Huntington's disease should be sought.

The social and cultural history should include information about education, literacy, and socioeconomic, ethnic, and cultural background, as well as information on recent life events and social support networks. As noted, these factors can affect the risk for dementia as well

as current performance on mental status tests.

The medication history is a critical component of the initial evaluation because drug toxicity is the most common cause of reversible dementia (Katzman, Lasker, and Bernstein, 1988). A wide range of drugs has been associated with cognitive changes (see Table 5). Given the large number of drugs that may cause cognitive changes, clinicians should consider any drug, including over-the-counter medications and alcohol, as potentially suspect. (Many patients do not think of nonprescription compounds as "medicine" or "drugs" and may need to be asked about them specifically, with examples, such as aspirin, as prompts.) Patients should be encouraged to bring all pills and medication bottles to the appointment.

> The history should be obtained from the patient and a reliable informant. (Strength of Evidence = C)

The informant should be a person familiar with the patient, for example, a family member or close friend. In addition to having memory loss, which limits the validity of subject reports, many patients with a dementing syndrome lack insight into the severity of their decline. This is especially true in patients with more severe impairment (Grut, Jorm, Fratiglioni, et al., 1993; McGlynn and Kaszniak, 1991). Informant reports can both corroborate and supplement reports of the affected person.

The importance of informant reports for establishing decline cannot be overstated (Berg, 1990; Henderson and Huppert, 1984). Informant reports also can provide important evidence for impairment in multiple cognitive domains. Notably, research concerning the retrospective accounts of dementia symptoms has shown that relatives' reports are reasonably reliable (La Rue, Watson, and Plotkin, 1992) and valid (Bayles and Tomoeda, 1991). Relatives' reports, however, can be influenced by the nature of the relationship to the patient. For example, La Rue and colleagues (1992) found that spouses of memory-impaired persons reported lower levels of impairment than did younger relatives. Thus, even though it may be difficult, it appears prudent to include more than one family informant or a family consensus approach to increase the accuracy of conclusions on the presence and range of cognitive impairments in those with suspected dementia.

Concern should be given to preserving a good doctor-patient relationship and for safeguarding the dignity of the patient. Patients should be informed that others may be interviewed. It is best to interview family members and other informants separately from the patient; family members are often very aware of deficits but may not be willing to discuss them in the presence of the patient for fear of upsetting him or her. Butler, Finkel, Lewis, et al. (1992) describe practical approaches to the initial office visit for a person suspected of having dementia who is accompanied by friends or family members. They emphasize the need to examine the patient alone and before the informant is interviewed to maintain the patient's dignity. Examining the patient alone also has implications for the development of a trusting physician-patient relationship (Greene, Majerovitz, Adelman, et al., 1994).

In evaluating informant reports, clinicians should be aware of the possibility of questionable motives, as well as the family's level of stress and fatigue, which frequently attend the process of diagnosing disturbing symptoms. For example, reports of behavioral and cognitive symptoms might be minimized if the family member is concerned that the patient will be denied admission to a nursing home. Conversely, symptoms could be exaggerated or even fabricated if the informant is motivated by financial gain or other issues.

Focused Physical Examination

A focused physical examination, including a brief neurological evaluation, is an essential part of the initial clinical assessment. It must be directed by the same principles that guide initial assessment of any medical condition; that is, life-threatening or rapidly progressing etiologies must be identified first. Life-threatening conditions include mass lesions, vascular lesions, and infections. Special attention should be paid to assessing for those conditions that cause delirium because delirium represents a medical emergency (see the section on Assessing for Delirium and Depression later in this chapter). The examination should include measurement of blood pressure and pulse, both lying and standing; assessment of vision and hearing; and evaluation for any evidence of cardiac failure, poor respiratory function, or problems in mobility or balance. A complete physical examination should be scheduled if not done at this visit.

All health care providers also must be alert to signs of a caregiver's abuse and neglect of patients with dementia. One recent study reported that severe physical abuse of the affected person occurs in approximately 20 percent of families (Paveza, Cohen, Eisdorfer, et al., 1992). Suspected abuse should be reported to the proper authorities.

Functional Status Assessment

A functional status assessment should be part of the initial clinical assessment (see Figure). The panel recommends the use of an explicit and standardized evaluation of functional

status (see Chapter 2, Functional Impairment section). Structured measures of functional performance, especially those that measure higher order social and instrumental activities, are particularly helpful when used in the context of a comprehensive evaluation for dementia (see Wilder, Gurland, Chen, et al., 1994). Performance testing of function can be helpful, particularly when informants are not available (Gurland, Cross, Chen, et al., 1994). Informant-based functional assessment scales, in particular, are important for evaluating complex or difficult cases (O'Connor, Pollitt, Hyde, et al., 1991) or persons who fall into "borderline" (Hershey, Jaffe, Greenough, et al., 1987) or "questionable" (Morris, McKeel, Storandt, et al., 1991) or "borderzone" (Wilder, Cross, Chen, et al., 1995) categories.

> The Functional Activities Questionnaire is useful in the initial assessment for functional impairment. (Strength of Evidence = A)

The Functional Activities Questionnaire (FAQ) (Pfeffer, Kurosaki, Harrah, et al., 1982), an informant-based measure, can provide critical information on an individual's functional abilities. This determination was made on the basis of meta-analyses conducted with data from studies that met the panel's criteria for inclusion. An informant provides performance ratings of the person being assessed (see Attachment E for information on administration and scoring of the FAQ). The FAQ is a good discriminator, with an average effect size of 2.46 for patients with mild-to-severe dementia and comorbid conditions. Effect size is a summary statistic that provides an index of an instrument's ability to discriminate between, in this case, subjects with and without dementia. An effect size of 2.46 for the FAQ corresponds to sensitivity and specificity values in the range of about 85 to 90 percent (Hasselblad and Hedges, 1995).

On the FAQ, an informant provides performance ratings of the target person on 10 complex, higher order functional activities (see Attachment E). Little evidence supports the use of the FAQ directly with the patient rather than (or in addition to) an informant. A recent study by Weinberger, Samsa, Schmader, et al. (1992) suggests that persons with very mild dementia may be able to provide valid reports of functional performance. This is confirmed by Wilder, Cross, Chen, et al. (1995). As a rule, however, every effort should be made to find a reliable informant.

Two measures of functional status were included in the meta-analysis -- the Katz ADL and the FAQ -- along with the other 50 psychological, neuropsychological, and mental status tests listed in Attachment C. Although the panel's recommendation of the FAQ is based on only a minimum number of studies, these studies yielded contrasts at Phase IV, the highest and thus most important level for the purpose of recommendations. Only 3 other tests of the total of 18 tests involved in Phase IV analyses had more than two contrasts: the MMSE (12), Wechsler Adult Intelligence Scale (WAIS) Digit Symbol (4), and WAIS Information (3). The remaining 15 tests contributed only two contrasts, as did the FAQ. However, the FAQ emerged as the best discriminator in these Phase IV analyses, and only its effect size of 2.46 was significantly different from (better than) the MMSE effect size of 1.78. Findings for the MMSE, although based on more studies, showed poorer specificity (ranging from .44 to .63) compared with a specificity of .80 for the FAQ.

It should be noted that neither the Katz ADL nor any other ADL or IADL scale had data that met Phase IV criteria. Furthermore, the FAQ was superior not only to the MMSE but also to all other 17 tests and measures in the Phase IV analyses. Together, these results support and lead to the panel's recommendation of the FAQ in the initial assessment of dementia. Recently, Pfeffer (1995) reported a larger, more representative study that gives further confirmation and validation.

Mental Status Assessment

The panel determined that universal or broad-band screening for Alzheimer's disease or related dementias among older adults was not warranted (see Chapter 1). In lieu of routine screening, the practitioner plays a pivotal role in being alert to the changes from baseline status that suggest the development of a dementing disorder in a patient and in recognizing the difference between such symptoms and the normal processes of aging.

Assessing the mental status of a person suspected of having dementia is the most critical component of the physical examination; a quantitative mental status examination should be part of the initial assessment. Ideally, this evaluation will provide a detailed cognitive profile of the patient. This approach, unfortunately, is impractical for most health care providers. However, in lieu of a comprehensive mental status examination, several brief, quantitative tests are available to assess mental status. These tests were developed to standardize the variety of individual approaches to the clinical evaluation of mental functioning.

Table 7. Components of commonly used brief mental status tests and requirements for testing

	MMSE	BIMC	BOMC	STMS
Components of cognition measured (listed in the DSM-IV criteria for dementia):				
-- Immediate memory	X			X
-- Short-term recall	X	X	X	X
-- Abstract thinking				X
-- Judgment				
-- Aphasia	X			
-- Apraxia	X			
-- Agnosia	X			
-- Constructional ability	X			X
Additional components of cognition measured:				
-- Concentration	X	X	X	X
-- Spatial ability, orientation	X	X	X	X
Requirements for testing:				
-- Verbal responses	X	X	X	X
-- Reading ability	X			
-- Writing ability	X			X
-- Mathematical ability	X			X
-- Vision	X			X
-- Motor control skills	X			

Note: MMSE = Mini-Mental State Examination; BIMC = Blessed Information-Memory-Concentration Test; BOMC = Blessed Orientation-Memory-Concentration Test; STMS = Short Test of Mental Status. Source: Adapted from White H, Davis PB. Cognitive screening tests: an aid in the care of elderly outpatients. J Gen Intern Med 1990;5;438-45. Copyright 1990, Society for Research and Education in Primary Care Internal Medicine. Used with permission.

Such instruments are composed of systematic, structured questions or tasks that can be readily scored at the time of administration. All of these instruments provide a brief examination of memory and orientation; some test a wider range of cognitive functions including visuospatial ability, language skills, and attention. Table 7 presents a summary of the components of cognition measured by each of several brief cognitive tests and of the requirements for testing, such as verbal ability or vision. Typically, a dichotomous, pass-fail system of scoring is employed, in which the total score for a test is compared with a clinically or empirically derived cutpoint. Attachment F provides instructions for administering and scoring selected mental status questionnaires.

The literature is growing for many of the brief mental status tests developed in the last 10 to 15 years. This evidence was submitted to meta-analysis as discussed in Chapter 1. To identify mental status tests that would be clinically useful across a wide spectrum of persons (Ransohoff and Feinstein, 1978), the panel adopted an analytic scheme of phases of evaluation for diagnostic marker tests (Nierenberg and Feinstein, 1988). Lower phases in the scheme involve relatively easy discriminations between case patients with severe dementia and healthy, high-functioning control subjects. Higher phases involve a wider

range of severity of illness (i.e., including patients with mild or early dementia and control subjects with comorbid conditions that mimic the performance of case patients). Attachment C presents the effect sizes results (in "D" columns), along with the number of contrasts and the Z values for 52 neuropsychological tests or subtests and functional status measures. Tests with Z scores in Attachment C of 1.96 or greater are significantly better than the MMSE (Folstein, Folstein, and McHugh, 1975) in distinguishing case patients from control subjects.

As seen in Attachment C, the great majority of studies and contrasts come from Phases II and III, where comorbidity among control subjects is absent. Only three tests have data at Phase III. In addition to the MMSE, the results in Attachment C indicate that the FAQ emerges as the best discriminator, especially at the highest level of discrimination difficulty, and its effect size is the only one significantly better than the MMSE. Several other mental status tests evaluated at the highest phase (IV) had effect sizes that were equivalent to the MMSE: the 26-item Blessed Information-Memory-Concentration (BIMC) test, the 6-item Blessed Orientation-Memory-Concentration (BOMC) test, and the Short Test of Mental Status (STMS) (the Selective Reminding-Total Words and the Symbol Digit Modalities are also equivalent to the MMSE).

Taken as a whole, the results of the meta-analyses from the most relevant contrasts -- those involving an expanded spectrum of case patients and control subjects with interfering or comorbid conditions -- indicate that four tests are largely equivalent in terms of their ability to differentiate between persons with and without dementia who have comorbid conditions of a general medical, psychiatric, and/or neurologic nature. Thus, any of these four mental status questionnaires -- the MMSE, the BIMC, the BOMC, or the STMS -- can be used to gather mental status information. The panel's meta-analyses from the most relevant contrasts available -- those involving an expanded spectrum of case patients and control subjects -- show that the various mental status tests are largely equivalent in their ability to differentiate between subjects with and without dementia. The MMSE (Folstein, Folstein, and McHugh, 1975) is the most widely used brief mental status examination in the United States, and the clinical and research literature on the MMSE is extensive and broad. However, clinicians who have experience using the BIMC, the BOMC, or the STMS could choose to continue using these tests.

> Currently, no single mental status test is clearly superior, and any of the tests recommended in the guideline may be used. (Strength of Evidence = A)

Because structured mental status tests can provide a quantitative baseline for monitoring the course of cognitive impairment, they can be useful in establishing a decline from previous cognitive levels. Repeated administration of the same mental status tests would be particularly valuable in reassessing mental status in persons found to have treatable delirium or depression on initial evaluation. Subsequent examination of these individuals may reveal improvement of cognition or, in the absence of significant improvement, may assist in confirming the presence of dementia. Currently, there is no evidence to suggest a timeframe for reassessment.

Whenever possible, clinicians should document the presence of decline from reports obtained from a close relative or another informant. In some instances, however, no reliable informant is available. In other cases, particularly in mild or early dementia, relatives may deny that the person has demonstrated cognitive deterioration, or they may minimize the extent of decline (Pollitt, O'Connor, and Anderson, 1989). Evidence for decline can be documented in these cases by comparing performance on a mental status test over time.

Because most brief mental status tests assess a range of cognitive functions, they also can be used to document multiple cognitive impairments, as required for a diagnosis of dementia. The MMSE is the most comprehensive of these tests. It examines orientation, attention, immediate and delayed memory, visuospatial ability, aphasia, agnosia, and apraxia. However, its approach is limited by differential sensitivity for various cognitive domains (Mitrushina and Satz, 1994). For instance, several studies show that the MMSE language items are too simple to detect mild impairment (Tombaugh and McIntyre, 1992), even though persons with mild dementia of Alzheimer's disease may have clear language impairments on more difficult language tasks (Bayles and Kaszniak, 1987). In one study of 76 subjects (about half of whom were diagnosed with Alzheimer's disease), four of the five MMSE language items showed very low (<15 percent) sensitivity, and three of these language items did not correlate with language measures of neuropsychological testing (Feher, Larrabee, and Crook, 1992). In this study, however, the MMSE language items did show reasonably high specificity.

On the basis of these studies, an MMSE finding of impairments in memory and at least one other cognitive area is consistent with the multiple cognitive deficits associated with dementia; however, a finding of impairment in memory only does not automatically rule out dementia.

Regardless of the test selected, its results should be interpreted in conjunction with the patient's signs and symptoms and with the functional status assessment. Brief mental status tests are important to the initial assessment of dementia, but they are not diagnostic and thus should not be used as stand-alone diagnostic tests.

This approach rests on the concept of incremental validity -- the notion that information from multiple, reliable sources enhances the validity of the assessment. Several studies provide support for this notion within the context of assessing dementia (Chaves and Izquierdo, 1992; Wilder, Gurland, Chen, et al., 1994). Wilder and associates (1994) showed, for example, that combining an informant's report of function with the results of a cognitive rating scale can yield sizable gains in specificity (reduction in the number of false-positives) without appreciable loss of sensitivity. These investigators also showed that, for the intermediate range of cognitive scores (i.e., neither very high nor very low), the additional information from a functional scale improves the prediction of dementia. This combination of an informant-based measure of functional performance with a brief cognitive rating scale has been widely endorsed in the dementia literature (Jorm and Korten, 1988; van der Cammen, van Harskamp, Stronks, et al., 1992; see also Gurland, Wilder, Chen, et al., 1995).

Confounding and Comorbid Conditions

> Factors such as visual impairment, sensory impairment, and physical disability should be assessed and considered in the selection of mental status tests. (Strength of Evidence = B)

Visual and auditory impairments, as well as various physical disabilities, may affect performance on mental status and neuropsychological tests (O'Connor, Pollitt, Hyde, et al. 1988; Peters, Potter, and Scholer, 1988). Individuals suspected of having dementia should be screened for visual and auditory impairment and for physical disability (e.g., neuromuscular disorder, severe arthritis) before mental status or other cognitive tests are administered. Visual and auditory deficits should be corrected, when possible, before testing. When visual or auditory deficits cannot be corrected or physical disability is present, the patient may need to be referred for neuropsychological evaluation employing tests that use his or her unimpaired sensory modalities and motor capacities. The MMSE in particular should not be used when the subject has impaired motor control because of the drawing and praxis portions of these tests; other tests (e.g., the BIMC) should be used. Care also should be taken when testing any older adult to ensure adequate illumination and contrast of visual stimuli and adequate volume and distinctiveness of auditory verbal stimuli.

Assessing for Delirium and Depression

> The clinician should seek evidence for delirium and depression during the initial clinical assessment. (Strength of Evidence = B)

During the focused history and physical examination, the clinician should seek any evidence of an acute confusional state or delirium and of dysphoric mood suggesting depression. These conditions can be mistaken for dementia or can coexist with dementia. They need to be addressed explicitly and promptly.

Although delirium is common in older persons with acute illnesses, it is underrecognized in clinical settings (Johnson, Kerse, Gottlieb, et al., 1992). Similarly, depression is the most common psychiatric illness in older persons (Blazer and Williams, 1980) and is also frequently underdiagnosed in this population, particularly where physical illness is present (Katzman, Lasker, and Bernstein, 1988).

Assessment for these conditions begins during the focused history and physical examination component of the initial clinical assessment. If either delirium or depression is present, it must be treated promptly. Assessment of the patient for possible dementia should continue if symptoms suggesting dementia remain after treatment for delirium or depression.

Delirium

Table 8. Diagnostic criteria for delirium due to general (more...)	Delirium and dementia can sometimes be difficult to differentiate clinically. In addition, the conditions may occur together, further complicating diagnosis. See Table 8 for characteristics of delirium as defined in DSM-IV. Although delirium, like dementia, is marked by global disturbances in cognition, it can be distinguished from dementia by disruptions of consciousness and attention, its clinical course, the development of clinical features over a short period of time (usually

hours to days), and significant fluctuations in the degree of cognitive impairment over the course of the day. A person who exhibits sudden onset of cognitive impairment, disorientation, disturbances in attention, decline in level of consciousness, or perceptual disturbances (e.g., hallucinations) is likely to have delirium rather than uncomplicated dementia.

Recognition and treatment of delirium are important because the underlying physical disorder, as well as the associated cognitive deficits and behavioral symptoms, can be sources of danger, distress, and mortality. The presence of delirium can indicate that medical illnesses or physiological abnormalities are affecting cerebral activity. Early recognition of delirium with mild symptoms may offer significant opportunities to prevent disability and irreversible deterioration. Levkoff, Evans, Liptzin, et al. (1992) suggest that acute onset of disturbances of consciousness, disorientation, and perceptual disturbances is associated with significant morbidity, even in the absence of the full-blown syndrome.

Delirium is a medical emergency requiring immediate further evaluation and treatment; some of the underlying causes (such as bacterial meningitis or hypoglycemia) can be fatal. Delirium is usually reversible if treated in a timely fashion.

Causes of delirium may be classified as predisposing and precipitating factors. Predisposing factors increase the risk of delirium and include increasing age, preexisting dementia, and other brain diseases such as stroke and Parkinsonism. Precipitating factors are the immediate causes of delirium and require urgent evaluation and treatment. Lipowski (1990) summarized the most frequently occurring precipitating causes. These include a number of common medical conditions and adverse effects of medications such as agents with anticholinergic (muscarinic blocking) activity, antipsychotic agents, antidepressants, digoxin, H_2-blocking agents, and antihypertensive agents (see also Table 5).

Delirium is common among elderly persons with acute illnesses. Prevalence rates are estimated in the range of 10 to 30 percent among medical inpatients and 7 to 52 percent among postsurgical patients, depending on clinical settings and the specific diagnostic criteria used (Levkoff, Cleary, Liptzin, et al., 1991). Delirium is also a common complication of chronic disease; prevalence rates in nursing homes have been estimated to be 6 to 7 percent (Rovner, German, Broadhead, et al., 1990).

Medical record reviews indicate that delirium is underrecognized in clinical settings (Johnson, Kerse, Gottlieb, et al., 1992). One potential problem in diagnosing delirium is that many clinicians may not know how to evaluate attention and level of consciousness. States of lethargy and stupor in which patients have difficulty in maintaining wakefulness should be readily recognized as symptoms of delirium, but more subtle disturbances in consciousness and attention that could identify persons needing urgent evaluations and treatment may not be recognized as such.

Recognition of dementia can be improved by using mental status tests to identify patients with cognitive impairment and by establishing the history of the onset and the degree of fluctuation in symptoms. Recent research has defined symptoms of delirium in operational terms, establishing the feasibility of using systematic methods for assessment at bedside or in the clinic. Anthony, LeResche, Von Korff, et al. (1985), for example, developed a method by which clinicians can rate "how well the patient kept his mind on interaction with the observer" and determined that these "global ratings of accessibility" are reliable and that they have high levels of both sensitivity (90 percent) and specificity (95 percent) against independent clinical diagnoses of delirium. More recently, Gottlieb, Johnson, Wanich, et al. (1991) assessed these symptoms through a combination of ratings of accessibility and measures of performance on brief tasks (e.g., spelling a word and stating the days of the week forward and backward). Albert, Levkoff, Reilly, et al. (1992) developed the Delirium Symptom Interview, which evaluated the disturbances of consciousness by administration of brief tests to patients (asking for days of the week and months of the year backwards) and by observations of behavior (e.g., staring into space unaware of the environment, inappropriate distraction by environmental stimuli). The Confusion Assessment Method and the Delirium Rating Scale are validated methods that distinguish between delirium and dementia (Inouye, van Dyck, Alessi, et al., 1990). Inouye, Viscoli, Horwitz, et al. (1993) developed a predictive model for delirium in hospitalized elderly patients.

Depression

Depression is often mistaken for dementia (Koskinen, 1992) and vice versa (Siegel and Gershon, 1986). Differentiation between depression and dementia is complicated by the fact that dementia can initially present as depression, sometimes in the absence of marked cognitive deficit (Reding, Haycox, and Blass, 1985). Conversely, depression may present as dementia. This has been referred to as "pseudodementia" (Kiloh, 1961) or, more recently, "depression-related cognitive dysfunction" (Stoudemire, Hill, Gulley, et al., 1989). Depression and dementia also may coexist. It has been estimated that 1 to 31 percent of persons diagnosed with a progressive dementing illness might actually be depressed and have associated memory deficits (Katzman, Lasker, and Bernstein, 1988). Depression can develop secondary to a dementing illness, such as Alzheimer's disease or vascular dementia, particularly in persons with less severe cognitive impairment.

Table 9. Diagnostic criteria for major depressive episode (more...)

Persons suspected of having dementia should be evaluated for depression. When the history is taken, symptoms consistent with depression as defined in DSM-IV (American Psychiatric Association, 1994) should be sought (see Table 9). If depression is suspected, further evaluation and appropriate treatment of depression should be undertaken, followed by reevaluation for dementia. The AHCPR-sponsored guideline for diagnosis and management of depression in the outpatient setting may be useful to clinicians in the assessment and treatment of depression (Rush, Golden, Hall, et al., 1993).

Accurate diagnosis of older adults who show concomitant signs of memory impairment and depression presents a continuing problem for physicians and other health care professionals. Depression in older persons, particularly those with physical illness, is frequently underdiagnosed. Depressed older adults are at high risk of suicide and mortality from other causes (National Institutes of Health Consensus Development Panel on Depression in Late Life, 1992). However, depression in older adults often responds to treatment with antidepressant medication, psychotherapy, electroconvulsive therapy, or all of the above (Benedict and Nacoste, 1990; Koenig and Blazer, 1992; National Institutes of Health Consensus Development Panel on Depression in Late Life, 1992).

Problems are also associated with misdiagnosing a progressive dementing illness as depression. In reviewing the literature, Siegel and Gershon (1986) concluded that 25 to 30 percent of older persons referred for evaluation and treatment of depression are ultimately diagnosed as having a progressive dementing illness. Inappropriate treatment for nonexistent depression in a person with a progressive dementia not only entails unnecessary expense but also can exacerbate the dementia because treatment with antidepressant medications that have anticholinergic properties may contribute to further confusion or memory impairment (Benedict and Nacoste, 1990; Harris, Gierz, and Lohr, 1989).

Historically, an "either-or" approach has been taken to the differential diagnosis of dementia and depression in older persons. As noted, however, dementia and depression often coexist (see, e.g., Table 2, for DSM-IV categories of Dementia with Depressed Mood, Codes 290.13 and 290.21). Depression can occur at any point in the progression of a dementing illness, but it is most frequent in those persons with less severe cognitive impairment (Merriam, Aronson, Gaston, et al., 1988; Reifler, Larson, and Hanley, 1982). Because persons with coexisting depression and Alzheimer's disease benefit from treatment of their depression (see Teri and Wagner, 1992), failure to diagnose and treat depression in a person with Alzheimer's disease may cause unnecessary emotional, physical, and social discomfort for both the patient and the family.

Assessing for depression is therefore an important part of the initial evaluation of any older adult suspected of cognitive impairment. This is particularly true for the person who presents with complaints of memory difficulty (as contrasted with the person who is brought in for evaluation by a spouse or other relative who suspects memory impairment) (Kahn, Zarit, Hilbert, et al., 1975; Larrabee and Levin, 1986). In addition to complaints of memory problems, some depressed older persons may show evidence of functional disability and impairment on tests of memory. Although changes in memory, attention, and executive function (i.e., goal formulation, planning, and execution of plans) are commonly associated with depression, marked visuospatial or language impairment would suggest a dementing process.

A substantial number of older adults may have clinically significant depressive symptoms that do not meet the full criteria for major depression listed in Table 9 (Blazer, Hughes, and George, 1987). The DSM-IV includes a category called Depressive Disorder Not Otherwise Specified for presentations that do not meet the full criteria for major depression but still cause clinically significant distress or major impairment. This diagnostic category may be appropriate for these patients.

Clinical Interview. The clinical interview is the mainstay for evaluating and diagnosing depression in older adults (National Institutes of Health Consensus Development Panel on Depression in Late Life, 1992). The DSM-IV provides some guidance on obtaining relevant interview information and observations for a given person. In applying the DSM-IV criteria for a major depressive syndrome, one should be aware that many of the somatic and behavioral symptoms could be related to physical conditions or behavioral changes that are common among older persons (Klerman, 1983). These symptoms include changes in sleep pattern and appetite, fatigue, behavioral slowing or agitation, and complaints of diminished ability to think or concentrate. In addition, many drugs taken by elderly persons for common medical conditions can induce depression, aggravate preexisting depression, or produce depression-related symptoms (Klerman, 1983; Salzman, 1992). Polypharmacy is common among older individuals and further complicates the situation because drug interactions also can produce depression or depression-related symptoms (Popkin and Tucker, 1992; Salzman, 1992), as well as contribute to cognitive dysfunction (see Table 5).

Instruments to Assess Depression. Brief self-report questionnaires can facilitate initial screening for depression-related symptoms. Several reviews comparing older-adult normative, reliability, and validity data from self-report depression screening instruments are

available (Fry, 1986; Gallagher, 1986; Kaszniak and Allender, 1985; Yesavage, 1986).

However, for persons suspected of having a dementing illness, standard screening instruments for assessing depression should be used with caution. Considerable difficulties are encountered in assessing for depression in older adults with known or suspected memory impairment (Kaszniak, Sadeh, and Stern, 1985; Raskind and Peskind, 1992; Rubin, Zorumski, and Burke, 1988). For example, memory difficulty, agitation, disrupted sleep-wake cycle, and personality changes such as apathy and increased dependence are classic symptoms of Alzheimer's disease that may be mistaken for depressive signs of poor concentration, decreased interest, changes in psychomotor activity, sleep disturbance, and fatigue. Depression-related symptoms may be common in the early stages of Alzheimer's disease and may occur in the absence of the full syndrome of clinical depression (Burke, Rubin, Morris, et al., 1988; Burns, 1991; Merriam, Aronson, Gaston, et al., 1988).

One self-report depression screening instrument, the Geriatric Depression Scale (GDS) (Brink, Yesavage, Lum, et al., 1982; Yesavage, Brink, Rose, et al., 1983), was developed specifically for use with older adults. It is reliable and valid for the assessment of depression in elderly outpatients, inpatients, and nursing home residents (Lesher, 1986; Parmelee, Katz, and Lawton, 1989; Scogin, 1987; Yesavage, Brink, Rose, et al., 1983). The GDS is a 30-item questionnaire, with clearly and simply phrased items and a "yes/no" response format that takes only 8 to 10 minutes to administer. The content focuses on mood and mood-related symptoms and excludes somatic items that may reflect physical illness in older persons. A score of 11 or greater is taken as an indication of possible depression. A 15-item short form of the GDS also may be useful for many purposes (Yesavage, 1988).

Although the GDS has merit as a screening instrument for depression in older adults with suspected memory impairment, the possibility of false-negative results must be considered. Several studies indicate that, in comparison with self-report instruments, collateral sources (such as spouses and other relatives) and trained clinical observers consistently report significantly higher frequencies of depression-related symptoms in Alzheimer's disease patients who have mild dementia (Burke, Rubin, Morris, et al., 1988; Mackenzie, Robiner, and Knopman, 1989; Miller, 1980; Rubin, 1990; Teri and Wagner, 1992). Thus, persons with Alzheimer's disease may report fewer depression-related symptoms than their clinicians or caregivers report. Conversely, Burke et al. (1988) suggest that collateral sources may have a "heightened awareness" of depression-related symptoms that occur in Alzheimer's disease and thus may be more likely to overreport them.

Considering the possibilities of observer bias in reporting depression-related symptoms, optimal depression screening in patients suspected of dementia should include information from both individual self-report and caregiver report, as well as direct clinician observation of the patient's behavior. Among those instruments appropriate for obtaining caregiver report of depression-related symptoms, the Hamilton Depression Rating Scale (HAM-D) has been used successfully in studies of Alzheimer's disease, and the Center for Epidemiological Studies-Depression Scale (CES-D) has been modified successfully as a caregiver report of patient depression (Teri and Wagner, 1992). The recently developed Columbia University Scale for Psychopathology in Alzheimer's Disease (CUSPAD) (Devanand, Miller, Richards, et al., 1992) is a broad measure of behavioral problems and appears promising. The CUSPAD is a brief semistructured instrument that can be administered by a trained lay interviewer to an informant in 10 to 25 minutes. The PRIME-MD procedure, developed by Spitzer, Williams, Kroenke, et al., 1994, was designed specifically to assist primary care practitioners in identifying psychiatric symptoms in their patients. Another promising new instrument is the Cornell Scale for Depression in Dementia (CSDD) (Alexopoulos, Abrams, Young, et al., 1988), a 19-item scale that requires a trained clinician to obtain information from both the patient and an informant. The AHCPR Clinical Practice Guideline, *Depression in Primary Care: Volume I. Detection and Diagnosis*(Rush, Golden, Hall, et al., 1993), also should be consulted.

Interpretation of Findings and Recommended Actions

This section presents recommendations based on the results of the initial clinical assessment for possible dementia. The mental and functional status tests each yield a discrete score that clinicians can compare with established cutpoints to arrive at a relatively gross, pass-fail decision for each test. (Cutpoints are provided in Attachment F for the MMSE; cutpoints have not yet been developed for other mental status tests.) These recommendations specifically address interpreting the results of these quantitative assessments and determining the most appropriate next steps. They provide a framework for making clinical decisions; the specific circumstances of each person should be considered in deciding the appropriate course of action (cf. Larson, Reifler, Sumi, et al., 1986).

If both mental and functional status tests are normal and no other concerns have been raised in the clinical assessment, reassurance by the treating health professional is recommended, together with a suggestion for reassessment in 6 to 12 months. If concerns persist despite normal mental

status and functional assessment results, referral for a second opinion or further clinical evaluation is appropriate. (Strength of Evidence = C)

Further clinical evaluation should be conducted if abnormal findings are obtained for both mental status and functional status tests. (Strength of Evidence = C)

Referral for neuropsychological, neurological, or psychiatric evaluation should be made if mixed results -- abnormal findings on the functional assessment with normal mental status performance or vice versa -- are obtained. (Strength of Evidence = C)

Three results are possible from the combination of findings from the mental status examination and functional status assessment: normal, abnormal, and mixed. Given the nature of symptoms that raise the possibility of dementia, referrals for neurological, psychiatric, or neuropsychological evaluation, depending on the findings of the initial assessment, are a common second step. Patients and family members may appreciate knowing the range of possible next steps in advance.

Normal: If findings from both the mental status test and the assessment of functional status are normal and no other concerns have been raised in the brief clinical evaluation, the patient and concerned associates (family or other) should be reassured, including a suggestion for reassessment in 6 to 12 months or whenever any further concerns develop. If, despite this reassurance, concern remains, referral for a second opinion or further clinical evaluation is indicated.

If the clinician, patient, or family member has concern about the adequacy of the mental status test, referral for further neuropsychological testing is appropriate. If there is concern about possible depression or other emotional problems despite the normal evaluation, referral for further psychiatric or psychological evaluation should be made. If there is concern about possible loss of social and instrumental functioning caused by a neurological disorder not detected in the functional test, referral to a neurologist should be made.

Abnormal: If abnormal findings are obtained for both mental status and functional status, this is sufficient probability that the patient has a dementing illness, and further clinical evaluation should be undertaken. This evaluation should include differential diagnosis, treatment, and ongoing care as indicated. Examples of resources for such further clinical evaluation are included in Attachment A. The procedures listed in this guideline have been identified as important in the basic assessment of patients with suspected dementia (Absher and Cummings, 1992; Larson, Reifler, Sumi, et al., 1986; Roth, 1993). As with all aspects of patient assessment, clinical judgment should dictate the selection of tests for any specific patient.

Laboratory tests may be appropriate when there is suspicion of specific medical conditions. However, a laboratory test should not be used as a screening procedure or as part of the initial assessment. Laboratory tests should be conducted only after (a) it has been established that the patient has impairment consistent with the definitions used in this guideline (i.e., in multiple domains, not lifelong, representing a decline from a previous level); (b) delirium and depression have been excluded; (c) confounding factors such as educational level have been considered; and (d) it is relevant to rule out a medical condition (Siu, 1991).

Mixed: Mixed results -- abnormal findings on the mental status test with no abnormalities in functional assessment or vice versa -- call for further evaluation. Abnormal results on only the mental status tests would call for more complete neuropsychological testing and -- depending on whether the results indicated possible neuropsychiatric or systemic neurological problems -- further referral to the appropriate specialist. Other situations that could give such a mixed picture include a person with lifelong borderline or retarded intellectual functioning who has learned to perform routine activities of daily living adequately, or a person with a dementing illness who is residing in an environment where sufficient functional supports mask evidence of significant functional impairment.

Alternatively, a person with high intelligence and education might have a score within the normal range on a mental status test, especially in early states of dementia, but would manifest a clear functional decline, especially on demanding tasks. Persons with declining function but normal mental status performance on the simple mental status test should have further neurological evaluation for systemic neurological diseases or psychiatric or psychological evaluation if evidence suggests depression or other emotional problems.

Because some individuals with dementia may minimize or flatly deny any problem for lack of insight or denial, establishing a cognitive baseline against which to evaluate the nature and magnitude of any cognitive declines is important. Reassessment is also needed to verify the original assessment of impairment. Because cognitive performance can vary from day to day, a judgment of cognitive impairment, especially in mild cases, often requires several examinations weeks or months apart to document a stable impairment. Reassessment also contributes to the documentation of cognitive performance over time, including documenting declines.

Determining the presence of dementia requires attention to both quantitative test results and clinical findings as obtained in the targeted history and physical examination. In diagnosing mild dementia, reliable informants' accounts of minor cognitive changes in a person suspected of dementia may be as important as (O'Connor, Pollitt, Hyde, et al., 1991) or more important than (Morris, McKeel, Storandt, et al., 1991) quantitative assessments, which can be insensitive to mild impairment.

> Confounding factors such as age, educational level, and cultural influences should be assessed and considered in the interpretation of mental status test scores. (Strength of Evidence = B)

Age and Educational Influences

For most mental status and neuropsychological tests, performance may be affected by both age and education (Tombaugh and McIntyre, 1992). In studies employing regression analyses (Brayne and Calloway, 1990; Uhlmann and Larson, 1991), education has accounted for more MMSE performance variance than other demographic variables including race, sex, and social class. In the largest normative study of the MMSE in the United States (Crum, Anthony, Bassett, et al., 1993), significant correlations were found between MMSE scores and both age and years of schooling. Crum and associates (1993) provide MMSE mean and percentile data, broken down by age and education. Age-specific MMSE norms have also been provided by Bleecker, Bolla-Wilson, Kawas, et al. (1988).

Many clinicians and investigators have assumed that the effects of education represent a psychometric bias, leading to misclassification of persons having different educational histories. Indeed, there is evidence that low education increases the probability of false-positive errors (misclassifying normal individuals as cognitively impaired), particularly when the person has fewer than 9 years of education (Anthony, LeResche, Niaz, et al., 1982; Murden, McRae, Kaner, et al., 1991).

There is also evidence that higher educational levels may result in increased false-negative errors (identifying a cognitively impaired person as unimpaired). For example, O'Connor, Pollitt, Hyde, et al. (1989) found that persons with false-negative MMSE identification of dementia had relatively high levels of education. The rate of decline in MMSE scores among persons with Alzheimer's disease has not been found to be associated with education (Burns, Jacoby, and Levy, 1991).

Despite the evidence that differing educational levels can be related to MMSE misclassification, education also may partially reflect the contribution of etiologic factors in the development of dementia (e.g., lower education could be associated with risk factors for vascular dementia such as hypertension) (Mortimer and Graves, 1993). Overall, however, the available data suggest that age- and education-stratified normative data, such as those provided by Crum, Anthony, Bassett, et al. (1993), are valuable in determining whether a particular individual's MMSE score is consistent with significant cognitive impairment.

Cultural Influences

Not only educational level, but also primary language, race, ethnicity, and cultural bias can affect performance on both mental status tests and particular neuropsychological tests. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD -- see Attachment D) has created a Spanish-language version of both its clinical and neuropsychological assessments (copies are available from CERAD), which have been administered to various Hispanic populations in the United States (Welsh, Butters, Mohs, et al., 1994). Escobar, Burnam, Karno, et al. (1986) studied more than 3,000 English- and Spanish-speaking residents of Los Angeles. Spanish-speaking persons were administered a Spanish version of the MMSE; English-speaking persons were administered the English version. Six of the MMSE items showed differential performance on the basis of language and ethnic status of the respondents. When these "ethnically biased" items were removed from the analysis, similar rates of cognitive impairment were found for Hispanics and non-Hispanics.

Neuropsychological tests have been found to be equivalently valid in differentiating persons with and without dementia in Hispanic and non-Hispanic populations. The possibility exists, however, that normative cutpoints for defining impairment or dementia differ. Lopez and Taussig (1991) found that unimpaired elderly Hispanic subjects scored lower on four

Wechsler Adult Intelligence Scale Revised (WAIS-R) subtests (i.e., Similarities, Vocabulary, Digit Span, and Block Design) (Wechsler, 1981) than unimpaired elderly non-Hispanic subjects. Comparison of scores for Hispanic and non-Hispanic patients with Alzheimer's disease on these same subtests found no significant differences, suggesting a "floor effect"; that is, performance of both groups was so low that differences were not detectable. When the two verbal WAIS-R subtests (Similarities and Vocabulary) were scored on the basis of culturally specific norms (scale scores of a Spanish version of the WAIS-R), the scores of the unimpaired Hispanic group were raised, eliminating the previous difference. The authors caution that the use of nonculturally specific norms may lead to underestimation of cognitive ability or, conversely, to overestimation of the level of cognitive impairment.

Loewenstein, Argüelles, Barker, et al. (1993) compared the neuropsychological test performance of 38 Hispanic and 38 non-Hispanic women who met criteria for probable or possible Alzheimer's disease. When their test results were compared, the Hispanic women tested in Spanish performed worse on the WAIS-R Digit Span and Comprehension tests as well as on the FAS Controlled Oral Word Association Test. The authors then divided their sample of patients based on a median split of the Fuld Object Memory Evaluation scores (Fuld, 1981), with below the median defining a moderately impaired group and above the median a mildly impaired group. Moderately impaired Hispanic patients scored worse on 5 of their 11 tests (WAIS-R Digit Span, Block Design, Object Assembly, Comprehension, and the FAS Controlled Oral Word Association Test) than their non-Hispanic counterparts. Furthermore, the mildly impaired Hispanic patients scored significantly worse on WAIS-R Digit Span than their non-Hispanic counterparts.

These studies suggest that several neuropsychological tests may place Hispanic persons and possibly members of other racial or ethnic groups at a disadvantage, particularly in the use of culturally inappropriate norms or cutpoints.

Tests of intellectual function used to assess cognitive performance or impairment must be interpreted according to norms established for levels of education and for the culture in which the test is administered. Because of the difficulties in comparing test results across cultures, norms for each test must be established in the culture in which it is applied.

Not only primary language, but also race and ethnicity (e.g., black versus white subjects of comparable educational level), social class, and socioeconomic status have been found to be related to MMSE scores in most studies examining these relationships (Tombaugh and McIntyre, 1992;for exception, see Murden, McRae, Kaner, et al., 1991). No information exists on whether identification of clinically significant cognitive impairment in minority racial and ethnic groups or in lower socioeconomic groups would be improved by the addition of IADL or neuropsychological test data.

Neuropsychological Testing

Objectives of Neuropsychological Testing

Formal neuropsychological assessment can address any or all of the following general aims (Albert and Moss, 1988; Bayles and Kaszniak, 1987; La Rue, 1992; Zec, 1993):

- Give information to patients, family members, and health care providers about the specific nature of strengths and deficits in cognitive functions.
- Assist in diagnosis, particularly in cases where the impairment is mild, the patient is of high premorbid intellectual ability, or there is an unusual combination of cognitive impairments.
- Contribute to recommendations for treatment and management of behavior problems.
- Provide a baseline measurement against which the effects of treatment or disease progression can be judged.

Available research suggests that neuropsychological assessment makes an important contribution to the identification of mild dementia, particularly when delayed recall is measured (Welsh, Butters, Hughes, et al., 1992). Because mental status tests such as the MMSE are less sensitive in detecting mild compared with moderate to severe cognitive impairment (for a review, see Tombaugh and McIntyre, 1992), neuropsychological testing may be particularly helpful when there is a history of apparent cognitive decline, but the results of a brief mental status test are normal.

In addition, the pattern of performance across neuropsychological tests has been found useful in identifying the presence of dementia among persons with high premorbid intellectual functioning, in discriminating patients with dementing illness from those with focal cerebral disease, and in differentiating among certain etiologies of dementia (La Rue, 1992; La Rue, Yang, and Osato, 1992; Parks, Zec, and Wilson, 1993). However, neuropsychological evaluation must be interpreted within the context of other clinical data, such as informant-based history of cognitive decline, evidence of impairment in IADLs, educational background, assessment for depression, sensory impairment, or factors other than dementia that may account for impaired performance.

Neuropsychological evaluation is recommended in the following circumstances:

1. When the mental status test, conducted as part of an initial assessment for possible dementia, is abnormal, but the functional assessment is normal.
2. When a family member expresses concern or there is suspicion about dementia, the results of mental status tests are within the normal range, and the patient has (a) more than a high school education or (b) an occupation that indicates high premorbid intelligence.
3. When mental status test results indicate cognitive impairment and the patient (a) has a low formal education, (b) shows evidence of long-term low intelligence (more than 10 years), (c) does not have adequate command of English for the test, (d) is of minority racial or ethnic background, (e) shows impairment in only one area of cognitive functioning on mental status tests, (f) does not have evidence of cognitive impairment for more than 6 months, or (g) does not show functional impairments. (Strength of Evidence = C)

Role of Neuropsychological Testing

Brief mental status tests usually have substantial false-negative rates in detecting cognitive impairment, especially if the impairment is caused by focal lesions of the right cerebral hemisphere (Nelson, Fogel, and Faust, 1986). The standardized tests used in neuropsychological assessment, however, have established reliability and sensitivity in the detection of cognitive deficits (see Grant and Adams, 1986; Kolb and Whishaw, 1990; Lezak, 1995; Spreen and Strauss, 1991). Appropriate neuropsychological tests may reveal subtle and circumscribed cognitive impairments in persons who show no evidence of deficits on brief mental status tests (see, e.g., Bondi, Kaszniak, Bayles, et al., 1993). The results of neuropsychological assessment instruments for the detection of mild dementia are correlated with the subject's level of education (Ganguli, Ratcliff, Huff, et al., 1991). They also can be affected by any of the following factors: physical disability, visual or auditory impairment, psychiatric illness (including depression), and limited facility with the English language (O'Connor, Pollitt, Hyde, et al., 1991).

Assessment in Various Cognitive Domains. Neuropsychological tests can examine performance across different domains of cognitive functioning, including orientation and attention, language functions, visual motor constructional ability (praxis), memory functions, abstract and conceptional reasoning, and executive functions. For this reason, they may be valuable in assessing for possible dementia in persons with high premorbid intellectual functioning when the clinician has a basis to determine that a loss of function has occurred (Naugle, Cullum, and Bigler, 1990). Furthermore, some evidence suggests that persons with mild dementia can improve their use of coping mechanisms and strategies to compensate for memory loss when they have information about their cognitive strengths and deficits derived from neuropsychological tests and given in the context of brief supportive counseling (LaBarge, Rosenman, Leavitt, et al., 1988).

Differentiation of Normal Aging and Causes of Dementia. Recent research has focused on the diagnostic utility of neuropsychological testing in differentiating dementia from normal aging and in distinguishing among different causes of dementia (Heaton, Grant, and Matthews, 1986; La Rue, 1992; La Rue, Yang, and Osato, 1992; Parks, Zec, and Wilson, 1993). For example, detailed neuropsychological assessment of memory function that distinguishes features such as learning and forgetting rates, recall versus recognition, and vulnerability to interference has been found useful in differentiating etiologies of dementia, such as Alzheimer's disease from Huntington's disease (Delis, Massman, Butters, et al., 1991).

Differentiation of Mild Dementia. In studies that address differentiation of healthy older adults from persons with very mild dementia caused by probable Alzheimer's disease, the most discriminating measures are those of recent memory, particularly delayed recall of newly learned material (Knopman and Ryberg, 1989; Morris, McKeel, Storandt, et al., 1991; Welsh, Butters, Hughes, et al., 1991). In one study (Morris, McKeel, Storandt, et al., 1991), postmortem evidence of Alzheimer's disease correlated completely with the results of psychometric differentiation of persons with mild cognitive impairment from normal older adults. Tests of recent memory also have been reported to show high sensitivity and specificity in discriminating mildly impaired persons who decline cognitively at 2-year reexamination from those who do not (Flicker, Ferris, and Reisberg, 1991).

Although these data appear encouraging for the application of neuropsychological testing (particularly of memory function) in detection of very mild dementia, high sensitivity may be achieved at the cost of a decrease in (or loss of) specificity. Not all persons with Alzheimer's disease have recent memory deficits as the most prominent initial deficits. In some patients with mild Alzheimer's disease, language or visuospatial abilities, including psychomotor performance, are the prominent features affected. Another early problem in some patients may be executive function (e.g., Becker, Bajulaiye, and Smith, 1992) or access to semantic memory (LaBarge, Balota, Storandt, et al., 1992; Storandt, Stone, and LaBarge, 1995).

Staging and Tracking. If a trigger (see Table 6) raises concern about change in cognitive performance, it is important to establish a baseline. A baseline measure greatly facilitates determination of cognitive decline over time.

The severity of recent memory deficits early in the course of Alzheimer's disease renders memory tests less useful than others for staging the severity of dementia across individuals (Welsh, Butters, Hughes, et al., 1992). Neuropsychological measures of other cognitive functions, such as recognition memory, verbal fluency, confrontation naming, and praxis, appear better for staging the severity of dementia or tracking its progression (Kaszniak, Wilson, Fox, et al., 1986; Welsh, Butters, Hughes, et al., 1992). When neuropsychological tests are carefully selected, they can play a valuable role in the evaluation of trials of medication or other interventions for persons with dementing illness (see Flicker, 1988).

Clinical Management. Identification of relatively intact cognitive function can be of assistance in developing plans for sharing daily responsibilities between the patient and others (see La Rue, Yang, and Osato, 1992). Conversely, neuropsychological documentation of specific deficits can direct caregivers to areas where the patient will require additional supervision or assistance. In a study of persons with probable Alzheimer's disease, Henderson, Mack, and Williams (1989) found that visuoconstructive deficits documented by neuropsychological tests significantly predicted "real world" spatial disorientation as reflected in caregiver reports of the patient's becoming lost, failing to recognize familiar environments, and wandering. Although research results to date have been mixed, neuropsychological evaluation also may be able to make contributions to decisions about whether a person can safely continue in potentially risky activities such as driving (for review, see Kaszniak, Keyl, and Albert, 1991).

Importance of Followup

After a referral has been made for further clinical evaluation, followup by the referring practitioner is important as is a clear explanation of what the symptoms may, or may not, indicate. Also important is reassurance that a referral does not mean loss of contact with what may be a trusted family physician; care will be coordinated and managed. Longitudinal followup after an assessment of declining mental function is probably the most important diagnostic procedure for differentiating Alzheimer's disease from normal aging. Thus, the mental status test should be repeated over a period of 6 to 12 months, and change or stability of the scores should be noted. For the MMSE, a change of four points a year is expected in persons with Alzheimer's disease. Test results and medical records should follow the patient from the specialist back to the referring practitioner.

For persons diagnosed with Alzheimer's disease or a related disorder, the progressive nature of associated cognitive impairment makes followup and continuity of care particularly relevant. Topics appropriate to discuss with the patient and family members include the patient's competence to drive and carry out other routine functions, such as cooking, that raise issues of safety; to maintain adequate nutrition and hygiene; to manage finances; and to supervise or care for grandchildren. Other relevant topics are financial, legal, and medical planning, including the execution of a durable power of attorney for health care. Patients and families may need time to absorb the diagnosis before they are ready to explore community resources, but making the information available (especially in take-home form) may be one of the most useful things practitioners can do.

Because the state of medical knowledge currently has little to offer patients and families coping with the distressing realities of dementia, referral to sources of practical information can be a lifeline. Community support groups, for example, can help by keeping isolation -- a common condition for family caregivers -- from becoming a psychologically debilitating problem (see Attachment D).

Conclusion

Although progress has been made in understanding certain aspects of Alzheimer's disease and many other dementing conditions, as of now most remain outside the realm of cure and prevention. Nevertheless, considerable benefits may accrue from early recognition of these conditions. This guideline is intended to help health care providers identify signs suggestive of a dementing disorder and follow a series of steps involved in assessment and referral, as warranted, with the goal of improving rates of early recognition.

This guideline focuses on recommendations for clinical activities related to recognition and

initial assessment, supported by a body of research literature and expert opinion. As a final note, however, the panel wishes to call attention to the broad ramifications of a diagnosis of probable dementia. Because dementias are disorders that destroy what many regard as the essence of personality and individuality, they are greatly feared. Dementing changes may advance inexorably but slowly over many years, creating not only deep emotional and psychological distress but also practical problems related to caregiving that often overwhelm the coping capacities of affected families. For this reason, Attachment D is included to help health care practitioners direct patients to sources of information about legal and financial planning, support groups, and other relevant services.

Acronyms

ADLs: Activities of daily living

AHCPR: Agency for Health Care Policy and Research

AIDS: Acquired immunodeficiency syndrome ALS Amyotrophic lateral sclerosis

APA: American Psychological Association

apoE: Apolipoprotein E

BIMC: Blessed Information-Memory-Concentration [Test]

BOMC: Blessed Orientation-Memory-Concentration [Test] (also "short OMC")

CERAD: Consortium to Establish a Registry for Alzheimer's Disease

CES-D: Center for Epidemiological Studies Depression Scale

CSDD: Cornell Scale for Depression in Dementia

CUSPAD: Columbia University Scale for Psychopathology in Alzheimer's Disease

DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, fourth edition

FAQ: Functional Activities Questionnaire GDS Geriatric Depression Scale

HAM-D: Hamilton Depression Rating Scale

HIV: Human immunodeficiency virus

IADLs: Instrumental activities of daily living

ICD-9-CM: International Classification of Diseases, 9th revision, Clinical Modification

MMSE: Mini-Mental State Examination

NINCDS: National Institute of Neurological and Communicative

ADRDA: Disorders and Stroke-Alzheimer's Disease and Related Dementias Association

PSMS: Lawton-Brody Physical Self-Maintenance Skills

SAILS: Structured Assessment of Independent Living Skills

STMS: Short Test of Mental Status

WAIS-R: Wechsler Adult Intelligence Scale Revised

Glossary

Activities of daily living (ADLs).: Self-maintenance skills such as dressing, bathing, toileting, grooming, eating, and ambulating.

Affective lability.: Rapidly changing or unstable expressions of emotion or mood.

Agnosia.: Loss or impairment of the ability to recognize, understand, or interpret sensory stimuli or features of the outside world, such as shapes or symbols.

Aphasia.: Prominent language dysfunction, affecting the ability to articulate ideas or comprehend spoken or written language.

Apraxia.: Loss or impairment of the ability to perform a learned motor act in the absence of sensory or motor impairment (e.g., paralysis or paresis).

Cognition.: The conscious faculty or process of knowing, including all aspects of awareness, perception, reasoning, thinking, and remembering.

Cognitive functions.: Mental processes, including memory, language skills, attention, and judgment (see also Table 6).

Comprehensive mental status examination.: Assessment of multiple cognitive functions that provides a detailed cognitive profile of the patient.

Confrontation naming.: The ability to name an object when shown a picture of it.

Delirium.: A temporary disordered mental state, characterized by acute and sudden onset of cognitive impairment, disorientation, disturbances in attention, decline in level of consciousness, or perceptual disturbances.

Dementia.: A syndrome of progressive decline in multiple areas (domains) of cognitive function eventually leading to a significant inability to maintain occupational and social performance.

Direct costs.: The expense of diagnostic, treatment, and care services.

Effect size.: A summary statistic that provides an index of the ability of a screening or test instrument to discriminate between, in this case, persons with and without dementia.

Episodic memory.: Memory of one's own experiences that is unique and localizable in time and space.

Executive functions.: Goal formulation, planning, and execution of plans.

Factor analysis.: A statistical procedure that is designed to determine if variability in scores can be related to one or more factors that are reliably influencing performance.

False-negative.: Erroneous finding of not having a particular medical condition (e.g., dementia) for a person who does have it.

False-positive.: Erroneous finding of a particular medical condition (e.g., dementia) for a person who does not have it.

Focused history.: A patient history confined to questions designed to elicit information related to cognitive impairment or a decline in function consistent with dementia and to document the chronology of the problems (Table 6).

Focused physical examination.: A physical examination that seeks to identify life-threatening or rapidly progressing illness, while paying special attention to conditions that might cause delirium. The examination typically includes a brief neurological evaluation as well as assessment of mobility and of cardiac, respiratory, and sensory functions.

Further assessment.: An additional evaluation, conducted after the initial assessment and intended to clarify information gleaned from that assessment, for the purpose of making a decision about the presence of a dementing disorder.

Incremental validity.: The notion that information from multiple, reliable sources enhances the validity of the assessment.

Indirect costs.: The expense of morbidity (the value of lost or reduced productivity of a patient, an unpaid caretaker, or both caused by illness) and mortality (the present value of future earnings lost because of premature death from disease).

Initial assessment (for dementia).: An evaluation conducted when the patient, clinician, or someone close to the patient first notices or mentions symptoms that suggest the presence of a dementing disorder. This evaluation includes a focused history, focused physical examination, examination of mental status and function, and consideration of confounding and comorbid conditions.

Instrumental activities of daily living (IADLs).: Complex, higher-order skills such as managing finances, using the telephone, driving a car, taking medications, planning a meal, shopping, and working in an occupation.

Meta-analysis.: Any systematic method that uses statistical analysis to integrate data from a number of independent studies.

Nonreversible dementias.: Term used to distinguish cognitive disorders that cannot be treated effectively to restore normal or nearly normal intellectual function from those that can.

Polypharmacy.: The administration of many drugs together.

Praxis.: The doing or performance of an action, movement, or series of movements.

Procedural memory.: Memory for certain ways of doing things or for certain movements.

Psychometric.: Relating to systematic measurement of mental processes; psychological variables such as intelligence, aptitude, and personality traits; and behavioral acts.

Reversible dementias.: Term used to distinguish cognitive disorders that can be treated effectively to restore normal or nearly normal intellectual function from those that cannot.

Semantic memory.: What is learned as knowledge; it is timeless and spaceless (e.g., the alphabet or historical data unrelated to a person's life).

Sensitivity (of a test instrument).: Ability to identify cases of a particular medical condition (e.g., dementia) in a population that includes persons who do not have it. Also called diagnostic sensitivity.

Specificity (of a test instrument).: Ability to identify those who do not have a particular medical condition (e.g., dementia) in a population that includes persons who do have it. Also called diagnostic specificity.

Standard deviation unit.: A measure of an approximate average of the amount by which each number in a set deviates from the mean of the set. The most commonly used measure of dispersion of statistical data.

Vascular dementia.: Dementia with a stepwise progression of symptoms, each with an abrupt onset, often in association with a neurologic incident. Also called multi-infarct dementia.

Visuospatial ability.: Capacity to produce and recognize three-dimensional or two-dimensional figures and objects.

Word fluency.: Ability to generate quickly a list of words that all belong to a common category or begin with a specific letter.

Contributors

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Specialty: Neuropsychology

Dr. Butters investigated the cognitive deficits associated with Alzheimer's disease and other forms of dementia. His work has helped delineate major memory disorders of Alzheimer's and Huntington's diseases. Dr. Butters also served as Director of the Neuropsychology Section of the Clinical Core of the UCSD National Alzheimer's Center. In addition, he was editor of the American Psychological Association's journal Neuropsychology and published more than 260 articles in peer-reviewed journals.

Marshal F. Folstein, MD
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Specialty: Psychiatry and Neurology

Dr. Folstein specializes in the cognitive and emotional effects of brain disease, including Alzheimer's disease. His research interests include the effects of psychoactive medications and the genetic basis of Alzheimer's disease. A member of several national task forces on Alzheimer's disease, Dr. Folstein serves on the editorial boards of numerous professional journals and has written or coauthored more than 160 research articles and book chapters.

Sid Gilman, MD
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Department of Neurology
University of Michigan Medical Center
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Specialty: Neurology

Dr. Gilman is a diplomate of the American Board of Psychiatry and Neurology, an academic neurologist, and a specialist in neurodegenerative diseases who performs both basic and clinical research. He is Director of the Michigan Alzheimer's Disease Research Center, Codirector of the Center's Community Outreach Education Program, and Director of the Michigan Dementia Program. Dr. Gilman has published numerous book chapters and abstracts as well as more than 300 articles in peer-reviewed journals.

Barry J. Gurland, FRCPhys (London), FRCPsych
John E. Borne Professor of Clinical Psychiatry
Director, Columbia University Stroud Center for Study of Quality of Life
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New York State Psychiatric Institute
New York, NY
Specialty: Geriatric Psychiatry

Dr. Gurland's research focuses on the boundaries of diagnosis and the interaction of physical and mental processes that produce impairments in the quality of life of persons in the latter half of life. He served as principal investigator of the United States-United Kingdom Cross National Diagnostic Project and currently shares leadership of a cross-cultural community study of Alzheimer's disease and its effects on objective and subjective functioning and other qualities of life. Dr. Gurland has published more than 150 papers in these research areas.

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Specialty: Social Work, Alzheimer's Education

Ms. Gwyther directs the Alzheimer's Family Support Program at the Duke University Center for Aging, a State-level central resource facility for Alzheimer's caregivers. She is a member of the U.S. Department of Health and Human Service's Advisory Panel on Alzheimer's Disease, has served on the Medical and Scientific Advisory Board of the Alzheimer's Association, and chairs the Social Research, Policy, and Practice section of the Gerontological Society of America. She is a Fellow of the Gerontological Society and previously served as the Practice Concepts section editor for its journal, The Gerontologist. Ms. Gwyther has published more than 50 journal articles, books, and manuals on Alzheimer's care.

Albert Heyman, MD
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Specialty: Neurology (Alzheimer's Disease)

Dr. Heyman is principal investigator of the Consortium to Establish a Registry for Alzheimer's Disease (CERAD), a nationwide project to develop standardized tests for the determination of Alzheimer's disease. He has published more than 200 papers and has served on the editorial boards of several journals, including Neurology, Stroke, Alzheimer's Disease and Related Disorders, and Journal of Geriatric Psychiatry and Neurology. He is a member of many advisory committees, as well as the American Academy of Neurology and the American Neurological Association. Dr. Heyman was honored at a National Institute on Aging Symposium on Vascular Dementia.

Alfred W. Kaszniak, PhD, ABPP
Professor of Psychology, Neurology, and Psychiatry
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Specialty: Clinical Neuropsychology

Dr. Kaszniak is a diplomate of the American Board of Clinical Neuropsychology and Director of Clinical Neuropsychology at the University of Arizona. His 3 books and more than 80 scientific papers, chapters, and reviews focus on neuropsychological aspects of aging and age-related disorders of the central nervous system, particularly Alzheimer's and Parkinson's diseases. He has served on the editorial boards of several journals and as an advisor to numerous national institutes and agencies concerned with aging and Alzheimer's disease. Dr. Kaszniak is also President of the Section on Clinical Geropsychology, Division of Clinical Psychology, American Psychological Association.

Ira R. Katz, MD, PhD
Professor of Psychiatry
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Specialty: Geriatric Psychiatry

Dr. Katz is Professor of Psychiatry and Director, Section of Geriatric Psychiatry, University of Pennsylvania and the Philadelphia Veterans Affairs Medical Center; Director of Psychiatric Research, Philadelphia Geriatric Center; and President of the American Association of Geriatric Psychiatry. He also serves as a member of the American Psychiatric Association's Committee on Long-Term Care and Treatment for the Elderly and has written numerous publications on issues related to geriatric psychiatry.

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Ms. Levy is a licensed occupational therapist, a Fellow of the American Occupational Therapy Association, an Associate Professor of Occupational Therapy at Temple University's College of Allied Health Professions, and a Faculty Associate of the Geriatric Education Center of Pennsylvania. She specializes in adult psychosocial dysfunction and geropsychiatry, including clinical experience in rehabilitation of patients with dementia. Ms. Levy has published widely and presented numerous workshops and seminars on dementia and its impact on individual behaviors, rehabilitation, and the family.

Nancy Emerson Lombardo, PhD
Senior Research Associate and Policy Specialist
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Boston, MA
Specialty: Alzheimer's Disease Caregiver Intervention Studies, Mental Health Practice and Policy in Long-Term Care

Dr. Lombardo, a founder of the Alzheimer's Association, led the development of its national chapter and public policy efforts, is vice-chair of its national board of directors, and is a board member of the local chapter. She has served on several national and State advisory boards related to Alzheimer's disease or nursing homes and as a board member of agencies serving minority elders. As a principal investigator, Dr. Lombardo has focused on improving services to elders with mental disorders, caregiver education and intervention programs, multicultural education and outreach, family-professional partnerships, dance therapy, and mental health of nursing home residents.

Nancy K. Orr-Rainey, MSG
Leavenworth, WA
Specialty: Program Development in Long-Term Care

Ms. Orr-Rainey owns a private consulting firm that specializes in program development for long-term care. Her clinical specialties include Alzheimer's disease, an area in which she has worked for more than two decades, rehabilitation, hospice, and adult day programming. She has assisted in and managed implementation of more than 100 specialty programs throughout the United States. When a family member was casually given a label of Alzheimer's disease without diagnosis, Ms. Orr-Rainey became an advocate of consumer education and quick, reliable screening for cognitive impairments.

Linda R. Phillips, PhD, RN, FAAN
Professor and Associate Dean for Research
University of Arizona College of Nursing
Tucson, AZ
Specialty: Gerontological Nursing

Dr. Phillips has been involved in research and writing about caring for the aged since 1978. The unifying theme of her work is the nature of the social processes involved in care, and her particular interests include the dynamics of family caregiving, elder abuse, and institutional care for elders with dementia or confusion. Dr. Phillips is the principal investigator of a National Institutes of Health study of the quality of family caregiving among Anglos and Mexican Americans and coprincipal investigator of an AHCPR-funded study of the effect of community health nursing interventions on the health of rural Mexican Americans.

Martha Storandt, PhD
Professor of Psychology and Neurology
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Specialty: Psychology of Aging

Dr. Storandt's research focuses on aging and Alzheimer's disease. She is Director of the Aging and Development Program in the Department of Psychology and Associate Director for Clinical Research for the Washington University Alzheimer's Disease Research Center. She also has served as editor-in-chief of the Journal of Gerontology, as a board member of the National Advisory Council for the National Institute on Aging, and as President of the Division on Adult Development and Aging of the American Psychological Association, of which she is a Fellow. Dr. Storandt recently coedited the book Neuropsychological Assessment of Dementia and Depression: A Guide for Clinicians.

Eric G. Tangalos, MD, FACP
Associate Professor of Medicine
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Specialty: Geriatrics

Dr. Tangalos is Director of Information Transfer for the Mayo Clinic Alzheimer's Disease Center and has been a consultant in the Mayo Clinic's Division of Community Internal Medicine since 1979. He is a Fellow of the American College of Physicians and of the American Geriatrics Society, and a Certified Medical Director. In addition, he has served as President of the Minnesota Association of Nursing Home Medical Directors and the American Medical Directors Association. Dr. Tangalos is one of two physicians appointed by President Clinton to the Advisory Committee of the 1995 White House Conference on Aging.

May L. Wykle, PhD, RN, FAAN
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Specialty: Geriatric Mental Health

Dr. Wykle is principal investigator of a 4-year study funded by the National Institute of Nursing Research, entitled "Black vs. White Caregivers Formal/Informal Service Use," and has been principal investigator on several research and training grants. She is also a Fellow of the American Academy of Nursing and of the Gerontological Society of America. In addition, she has published 75 articles and book chapters and edited 6 books. Dr. Wykle is a recent recipient of a 3-year National Institute on Aging Geriatric Leadership Academic Award.

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Attachments

Attachment A. Resources for Further Evaluation

American Academy of Neurology. Practice parameters for diagnosis and evaluation of dementia (summary statement): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology.* 1994; 44: 2203–6. [PubMed]

Clarfield AM. The reversible dementias: do they reverse?
Ann Intern Med. 1988; 109: 476–86. [PubMed]

Differential diagnosis of dementing diseases. NIH Consensus Statement 1987 July 6-8. 6(11):1-9.

McKhann G, Drachman D, Folstein M, et al. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology.* 1984; 34: 939–44. [PubMed]

U.S. Department of Veterans Affairs. Dementia: guidelines for diagnosis and treatment, 1989 (revised). VA Publication No. IB 18-3. pp. –.

Attachment B. Instruments for Which Specific Literature Searches Were Conducted

Mental-Status Exams
Mini-Mental State Examination (MMSE)
Mental Status Questionnaire (MSQ)
Short Portable Mental Status Questionnaire (SPMSQ)
Blessed Information-Memory-Concentration Test (BIMC)
Abbreviated Mental Test (AMT)
Blessed Orientation-Memory-Concentration Test (BOMC)
Functional Capacity Measures
Blessed Dementia Rating Scale (BDRS)
Instrumental Activities of Daily Living (IADL)
Short-CARE
Lawton-Brody Physical Self-Maintenance Scale (PSMS)
Psychogeriatric Dependency Rating Scale
Functional Activities Questionnaire (FAQ)
Verbal and Visual Memory Tests
Selective Reminding (SR) Procedures, immediate
Selective Reminding (SR) Procedures, delayed
Word List Recall (CERAD), delayed
Delayed Spatial Recognition Span
Benton Visual Retention Test, delayed
Constructional Ability/Praxis
Clock Drawing Tests

Attachment C. Comparison of Mental and Functional Status Tests According to Three Phases of Discrimination Difficulty

	Phase II			**Phase III**			**Phase IV**		
	# Contr	D	Z	# Contr	D	Z	# Contr	D	Z
Mini-Mental State Examination (MMSE)	**8**	**4.08**	**0.00**	**19**	**2.40**	**0.00**	**12**	**1.78**	**0.00**
26-item BIMC (Katzman et al., 1983)	**5**	**4.72**	**0.62**	**2**	**3.75**	[*]**3.29**	**2**	**2.49**	**1.36**
6-item BOMC (Katzman et al., 1983)	**2**	**6.51**	**1.36**	*1*	*3.79*		**2**	**1.63**	**-0.60**
Short Test of Mental Status (STMS)							**2**	**2.01**	**0.39**
Mental Status Questionnaire	*1*	*3.41*		*1*	*2.11*		*1*	*1.81*	
Short Portable MSQ	*1*	*10.09*		**2**	**2.18**	**-0.22**	*1*	*1.77*	
Functional Activities Questionnaire							**2**	**2.46**	[*]**2.81**
Associate Learning Recall of WMS				**3**	**1.36**	**-2.90**			
Assoc Learning Recall-Easy Pair (WMS)	*1*	*2.93*		*1*	*1.25*		*1*	*0.67*	
Assoc Learning Recall-Hard Pair (WMS)	*1*	*2.23*		*1*	*1.75*		*1*	*1.65*	
Delayed Logical Memory (WMS)	**3**	**3.76**	**-0.29**	**4**	**3.41**	[*]**2.04**	*1*	*2.34*	
Delay Visual Reproduction (WMS)	**3**	**2.57**	**-2.05**	**3**	**2.62**	**0.49**			
Digit Span Backward				*1*	-		*1*	*0.21*	

(WMS)				*1*	*0.16*		*1*	*0.21*	
Digit Span Forward (WMS)				**2**	**0.07**	**-6.40**	*1*	*0.54*	
Immediate Logical Memory (WMS)	**3**	**2.83**	**-1.85**	**8**	**2.08**	**-0.79**	*1*	*1.58*	
Mental Control (WMS)				*1*	*-0.05*		*1*	*0.07*	
Visual Reproduction (WMS)	**3**	**2.61**	**-2.04**	**4**	**1.28**	**-2.73**	*1*	*0.75*	
Verbal Fluency (Animals)	**2**	**3.29**	**-0.88**	**6**	**1.87**	**-1.36**			
Verbal Fluency (F)				**2**	**2.14**	**-0.61**	*1*	*0.50*	
Word Fluency (S)							*1*	*0.80*	
COWA (FAS)	**3**	**2.28**	**-2.17**	**6**	**1.69**	**-1.85**			
Blessed Dementia Scale	**3**	**2.96**	**-0.81**	**2**	**2.38**	**-0.06**	*1*	*0.55*	
Supermarket List Gen Test (DRS)				**2**	**2.83**	**1.09**	*1*	*1.54*	
BVRT-Form C-Number Correct	*1*	*1.02*		**3**	**1.94**	**-1.33**			
BVRT-Form C-Number Errors	*1*	*1.15*		*1*	*2.03*		*1*	*0.82*	
BVRT Copying-Number Correct	*1*	*0.75*		*1*	*0.35*				
BVRT Copying-Number Errors	*1*	*0.75*					*1*	*0.60*	
Selective Reminding-Total Words	*1*	*3.20*		**3**	**2.48**	**0.11**	**2**	**2.75**	**1.28**
Trailmaking Test-Part A				**3**	**1.28**	**-2.23**	*1*	*0.69*	
Trailmaking Test-Part	*1*	*4.08*		**3**	**1.98**	**-0.61**			
Porteus Maze Test	*1*	*3.11*		**2**	**2.42**	**0.01**			
Symbol Digit Modalities				*1*	*2.68*		**2**	**1.82**	**0.19**
Block Design (WAIS)	*1*	*2.93*		**2**	**1.48**	**1.48**	**-2.57**	**1.20**	**-1.30**
Comprehension (WAIS)				*1*	*1.64*		**2**	**0.98**	**-3.56**
Digit Span Forward (WAIS)	*1*	*1.81*		**4**	**0.77**	**-4.33**	**2**	**0.88**	**-2.63**
Digit Symbol (WAIS)				**2**	**1.21**	**-2.80**	**4**	**0.84**	**-3.00**
Information (WAIS)				*1*	*1.43*		**3**	**1.20**	**-2.09**
Picture Completion	*1*	*3.14*		*1*	*1.74*		**2**	**1.12**	**-2.73**

(WAIS)	*1*	*3.14*		*1*	*1.74*		**2**	**1.12**	**-2.93**
Similarities (WAIS)	**4**	**1.79**	**-4.69**	**3**	**0.47**	**-3.39**	**2**	**1.11**	**-2.98**
Vocabulary (WAIS)	**6**	**2.66**	**-1.66**	**5**	**1.97**	**-0.57**	**2**	**1.02**	**-3.38**
Block Design (WAIS-R)	**2**	**1.96**	**-4.34**	*1*	*1.53*		**2**	**1.18**	**-1.81**
Abbreviated Mental Test							**2**	**0.67**	**-2.60**
Kendrick Object Learning Test				*1*	*3.68*		**2**	**1.60**	**-0.18**
Kendrick Digit Copying Test				*1*	*0.62*		*1*	*1.05*	
Temporal Orientation				**2**	**0.98**	**-4.47**			
Token Test				**2**	**1.27**	**-2.44**			
Benton Test of Facial Recognition	*1*	*1.16*		**6**	**1.08**	**-4.30**	*1*	*2.08*	
Boston Naming Test	*1*	*2.87*		**6**	**1.76**	**-1.79**	*1*	*1.18*	
Category Retrieval	*1*	*16.65*		*2*	**4.71**	**1.11**			
Bender-Gestalt Test				*1*	*0.97*				
Cognitive Capacity Screening Exam				*1*	*1.82*		*1*	*2.02*	
Katz ADL	*1*	*6.48*		*1*	*7.80*				

Source: Guideline panel.
Notes: Data extracted from studies and assembled by guideline panel. Analytic scheme adapted from Nierenberg AA, Feinstein AR. How to evaluate a diagnostic marker test. Lessons learned from the rise and fall of dexamethasone suppression test. JAMA 1988; 259(11):1699-1702.
Tests with Z scores of 1.96 or higher are significantly better than the "reference" test (MMSE) in distinguishing case patients from control subjects.
Numbers in boldface are randomized average effect size (RAVD); numbers in italics are mean effect size (D).
ADL = Activities of Daily Living Scale; BIMC = Blessed Information-Memory-Concentration Test; BOMC = Blessed Orientation- Memory-Concentration Test; BVRT = Benton Visual Retention Test; COWA = Controlled Oral Word Association; DRS = Dementia Rating Scale; MSQ = Mental Status Questionnaire; WAIS = Wechsler Adult Intelligence Scale; WAIS-R = Wechsler Adult Intelligence Scale Revised; WMS = Wechsler Memory Scale
Phase II = moderate to severe dementia in case patients, no comorbidity in control subjects. Phase III = mild to severe dementia in case patients, no comorbidity in control subjects. Phase IV = mild to severe dementia in case patients, comorbidity in control subjects.
Contr = control;
D = effect size;
[2]Z = (test x minus MMSE) divided by square root of (SEtest x plus SEMMSE)
[*] p less than .05 one-tailed.

Attachment D. Resources for Health Professionals, Patients, and Families

When a diagnosis of dementia is made, the patient and family members have serious issues to consider. Although followup beyond this point is desirable, it cannot be ensured. For this reason, the visit during which the diagnosis is given is an appropriate time for the clinician to mention relevant issues, which include but are not restricted to long-term financial, legal, and medical planning. The following list of resources can be helpful to families when they are ready to confront the many implications of a diagnosis of dementia. A consumer version of this guideline is also available (see inside back cover for ordering information).

Administration on Aging

The Administration on Aging (AoA) coordinates delivery of services specified by the Older

Americans Act. Services are coordinated and provided through 57 State agencies and 657 areas.

Agencies on Aging (AAAs). The range of services provided by each AAA varies, but all include nutrition services, access services, in-home services, and community services.

Addresses and phone numbers of State and area AAAs may be obtained from the national office:

Administration on Aging
Department of Health and Human Services
330 Independence Avenue, SW
Washington, DC 20201
(202) 619-1006, (202) 619-7586 fax
Internet address: gopher://gopher.os.dhhs.gov/11/dhhs/aoa/aoa

The Elder Care Locator provides a toll-free access number to locate State agency networks: 800-667-1116.

Alzheimer's Disease Centers

The National Institute on Aging, a component of the National Institutes of Health, supports 28 Alzheimer's Disease Centers across the country. This program provides clinical services, conducts basic and clinical research, disseminates professional and public information, and sponsors educational activities. A growing number of satellite clinics associated with this program are helping to expand diagnostic and treatment services in rural and minority communities and collect research data from a more diverse population. For information, contact the ADEAR Center (see below).

Alzheimer's Association

The Alzheimer's Association is a national voluntary organization with 220 local chapters and more than 2,000 support groups. The Alzheimer's Association funds research, promotes public awareness, advocates legislation for patients and families, and provides support services, including support groups, adult day care programs, respite care programs, and telephone helplines through its national, local chapter, and volunteer network.

Alzheimer's Association,
919 North Michigan Avenue, Suite 100
Chicago, IL 60611-1676
(312) 335-8700, 800-272-3900 for information and local chapter referrals nationwide (24-hour telephone line)
Internet address: http://www.alz.org

Alzheimer's Disease Education and Referral Center

The Alzheimer's Disease Education and Referral (ADEAR) Center, a service of the National Institute on Aging, provides information and publications on Alzheimer's disease for health professionals, people with Alzheimer's disease and their families, and the public. The ADEAR Center serves as a national resource for information on diagnosis, treatment issues, patient care, caregiver needs, long-term care, education, research, and ongoing programs. In addition, the Center provides referrals to national and State resources. For information, contact:

Alzheimer's Disease Education and Referral Center
P.O. Box 8250
Silver Spring, MD 20907-8250
800-438-4380
Internet address: adear@alzheimers.org

The Corporation for National Service

The Corporation for National and Community Service is a public corporation that administers Federal service programs, including AmeriCorps, the Foster Grandparent Program, and the Senior Companion Program (SCP), which provides supportive services to adults with physical, emotional, and health limitations. A major emphasis of the SCP is preventing or delaying institutionalization. Foster Grandparent volunteers work with children, including those with disabilities. AmeriCorps members address a range of local health issues.

The address and phone number for regional offices may be obtained through the main office in Washington, DC.

Corporation for National Service
Office of Public Liaison
1201 New York Avenue, NW
Washington, DC 20525
(202) 606-5000

Other Resources

American Association of Retired Persons (AARP), Washington, DC, (202) 434-2277; 800-424-3410.
AARP Pharmacy Price Quote Center, 800-456-2226
American Bar Association Commission on Legal Problems of the Elderly, Washington, DC, (202) 662-8690
Children of Aging Parents, Levittown, PA, (215) 945-6900
Consortium to Establish a Registry for Alzheimer's Disease (CERAD), Durham, NC, (919) 286-6406 or 6405 National Association for Continence, Spartanburg, SC, 800-BLADDER (800-252-3337)
Insurance Consumer Helpline, Washington, DC, 800-942-4242 Medicare Hotline, Baltimore, MD, 800-638-6833
Medicare Beneficiaries Defense Fund, New York, NY, (212) 869-3850; 800-333-4114 National Citizens' Coalition for Nursing Home Reform, Washington, DC, (202) 332-2275 National Hospice Organization, Arlington, VA, (703) 243-5900; 800-658-8898 National Parkinson's Foundation, 800-327-4545, Miami, FL (East Coast); and 800-522-8855, Encino, CA (West Coast) National Stroke Association, Englewood, CO, (303) 771-1700; 800-STROKES.
Social Security Information, 800-772-1213 (open 7 am-7 pm in all time zones) U.S. Department of Veterans Affairs, Regional Office, Veterans Assistance, Washington, DC, (202) 418-4343; 800-827-1000.

Attachment E. Functional Activities Questionnaire (FAQ): Administration and Scoring

The FAQ is an informant-based measure of functional abilities. Informants provide performance ratings of the target person on 10 complex, higher-order activities.

Individual Items of the Functional Activities Questionnaire

1. Writing checks, paying bills, balancing checkbook.
2. Assembling tax records, business affairs, or papers.
3. Shopping alone for clothes, household necessities, or groceries.
4. Playing a game of skill, working on a hobby.
5. Heating water, making a cup of coffee, turning off stove.
6. Preparing a balanced meal.
7. Keeping track of current events.
8. Paying attention to, understanding, discussing TV, book, magazine.
9. Remembering appointments, family occasions, holidays, medications.
10. Traveling out of neighborhood, driving, arranging to take buses.

The levels of performance assigned ranged from dependence to independence, and are rated as follows:

- Dependent = 3
- Requires assistance = 2
- Has difficulty but does by self = 1
- Normal = 0

Two other response options can also be scored:

- Never did [the activity], but could do now = 0
- Never did and would have difficulty now = 1

A total score for the FAQ is computed by simply summing the scores across the 10 items. Scores range from 0 to 30. A cutpoint of "9" (dependent in three or more activities) is recommended.

Source: Pfeffer RI, Kurosaki TT, Harrah CH, et al. Measurement of functional activities of older adults in the community. J Gerontol 1982;37:323-9. Copyright 1982, Gerontological Society of America. Used with permission.

1. Mini-Mental State Examination

Maximum Score	Score	
		Orientation
5		What is the (year) (season) (date) (day) (month)?

5		Where are we: (state) (county) (town) (hospital) (floor)
		Registration
3		Name 3 objects: 1 second to say each. Then ask the patient all 3 after you have said them. Give 1 point for each correct answer. Then repeat them until he learns all 3. Count trials and record. Trials:
		Attention and Calculation
5		Serial 7's. 1 point for each correct. Stop after 5 answers. Alternatively spell "world" backwards.
		Recall
3		Ask for the 3 objects repeated above. Give 1 point for each correct.
		Language
		• Name a pencil and watch (2 points). • Repeat the following: "No ifs, ands or buts" (1 point). • Follow a 3-stage command: "Take a paper in your right hand, fold it in half, and put it on the floor" (3 points). • Read and obey the following: Close your eyes (1 point). • Write a sentence (1 point). • Copy design (1 point).
	Total Score	
		Assess level of consciousness along a continuum: Alert Drowsy Stupor Coma

Instructions for Administration of Mini-Mental State Examination

Orientation

1. Ask for the date. Then ask specifically for parts omitted, e.g., "Can you also tell me what season it is?" One point for each correct.
2. Ask in turn "Can you tell me the name of this hospital?" (town, county, etc.). One point for each correct.

Registration

Ask the patient if you may test his memory. Then say the names of 3 unrelated objects, clearly and slowly, about one second for each. After you have said all 3, ask him to repeat them. This first repetition determines his score (0-3) but keep saying them until he can repeat all 3, up to 6 trials. If he does not eventually learn all 3, recall cannot be meaningfully tested.

Attention and Calculation

Ask the patient to begin with 100 and count backwards by 7. Stop after 5 subtractions (93, 86, 79, 72, 65). Score the total number of correct answers.

If the patient cannot or will not perform this task, ask him to spell the word "world" backwards. The score is the number of letters in correct order, e.g., dlrow = 5, dlorw = 3.

Recall

Ask the patient if he can recall the 3 words you previously asked him to remember. Score 0-3.

Language

Naming: Show the patient a wrist watch and ask him what it is. Repeat for pencil. Score 0-2.

Repetition: Ask the patient to repeat the sentence after you. Allow only one trial. Score 0 or 1.

3-Stage command: Give the patient a piece of plain blank paper and repeat the command. Score 1 point for each part correctly executed.

Reading: On a blank piece of paper print the sentence "Close your eyes", in letters large enough for the patient to see clearly. Ask him to read it and do what it says. Score 1 point only if he actually closes his eyes.

Writing: Give the patient a blank piece of paper and ask him to write a sentence. Do not dictate a sentence, it is to be written spontaneously. It must contain a subject and verb and be sensible. Correct grammar and punctuation are not necessary.

Copying: On a clean piece of paper, draw intersecting pentagons, each side about 1 in., and ask him to copy it exactly as it is. All 10 angles must be present and 2 must intersect to score 1 point. Tremor and rotation are ignored.

Estimate the patient's level of sensorium along a continuum, from alert on the left to coma on the right.

Median Mini-Mental State Examination Score by Age and Educational Level

	Education				
	0-4y	5-8y	9-12y	>=12y	Total
18-24	23	28	29	30	29
25-29	23	27	29	30	29
30-34	25	26	29	30	29
35-39	26	27	29	30	29
40-44	23	27	29	30	29
45-49	23	27	29	30	29
50-54	23	27	29	29	29
55-59	22	27	29	29	29
60-64	22	27	28	29	28
65-69	22	28	28	29	28
70-74	21	26	28	29	27
75-79	21	26	27	28	26
80-84	19	25	26	28	25
>=85	20	24	26	28	25
Total	22	26	29	29	29

Source: Adapted from Crum RM, Anthony JC, Bassett SS, et al. Population-based norms for the mini-mental state examination by age and educational level. JAMA 1993;269:2386-91. Copyright 1993, American Medical Association. Used with permission.

2. The Blessed Orientation-Memory-Concentration (BOMC) Test

Overview

The six-item Blessed Orientation-Memory-Concentration (BOMC) test was developed by Katzman, Brown, Fuld, et al. (1983) from the longer (29-item) Blessed Information-Memory-Concentration (BIMC) test (Blessed, Tomlinson, and Roth, 1968). Katzman and colleagues (1983) selected 6 of the original 29 BIMC items based on a series of statistical analyses. The scores from each of the six items are multiplied as detailed below to yield a weighted score. Possible total scores on the BOMC range from 0 (all items answered correctly) to 28 (all items answered incorrectly). Weighted error scores greater than 10 are consistent with dementia, according to Katzman and colleagues.

The Blessed Orientation-Memory-Concentration (BOMC) Test

Items		Maximum error	Score		Weight
1.	What year is it now?	1		x 4 =	
2.	What month is it now?	1		x 3 =	
memory phrase:	Repeat this phrase after me: John Brown, 42 Market Street, Chicago				
3.	About what time is it? (within 1 hour)	1		x 3 =	
4.	Count backwards 20 to 1	2		x 2 =	
5.	Say the months in reverse order	2		x 2 =	
6.	Repeat the memory phrase	5		x 2 =	

Score of 1 for each incorrect response; maximum weighted score = 28
Source: Katzman R, Brown T, Fuld P, et al. Validation of a short orientation-memory-concentration test of cognitive impairment. Am J Psychiatry 1983;140:734-9. Copyright 1983, American Psychiatric Association. Used with permission.

3. The Blessed Information-Memory-Concentration (BIMC)Test

"Now I'd like to give you a short memory test that will take about five minutes. Some questions will be easy, some will be more difficult. Are you ready?"

The Blessed Information-Memory-Concentration (BIMC)Test

Correct	Error	
0	1	1. Name
0	1	2. Age
0	1	3. When born
0	1	4. Where born
0	1	5. Name of this place
0	1	6. What street is it on
0	1	7. How long have you been here (How long today)
0	1	8. Name of this city
0	1	9. Today's date
0	1	10. Month

0	1	11. Year
0	1	12. Day of week
0	1	13. Part of day
0	1	14. Time (Best guess) (Actual time:)
0	1	15. Season
Repeat this phrase after me: John Brown, 42 Market Street, Chicago.		
0	1	16. Mother's first name
0	1	17. Name of one school you attended
0	1	18. What kind of work have you done
0	1	19. Who is the president now
0	1	20. Who was the last president
0	1	21. Date of World War I
0	1	22. Date of World War II
0	1	23. Months of the year backwards. (Start with December) D N O S A Jl Jn M Ap M F Ja
0	1	24. Count from 1 to 20
0	1	25. Count backwards 20 to 1: 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1
0 1 2 3 4 5		26. Recall name and address: John Brown 42 Market St., Chicago (Cue with "John Brown" only. Score up to 5 errors)
TOTAL SCORE:		(The sum of the scores for all 26 questions. Total number of errors.)

Instructions for Scoring of the Blessed Information-Memory-Concentration (BIMC) Test

Information Test	
Score each item "1" for incorrect response; "0" for correct response.	
Item 5:	Possible answers include: home, hospital, etc.
Item 7:	Answer can be given in number of hours, days, etc.
Item 8:	The date must be the actual date of the month, within a day, e.g., the 16th, 5th, etc.
Item 13:	One of the following must be selected: morning, afternoon, evening, night.
Item 14:	Score as correct if within one hour of the actual time.
Memory Test	
Score each item "1" for incorrect response, "0" for correct response (except Item 27, see below).	
Item 3:	The month and year must both be given correctly.
Item	City and state must be given; town is optional. If foreign born, country is

4:	sufficient.
Item 19:	The name of the current president must be given; the last name is sufficient.
Item 20:	The name of the past president must be given; the last name is sufficient.
Item 21:	One of the years WWI took place must be given: 1914-1918.
Item 22	One of the years WWII took place must be given: 1939-1945.
Item 26:	If no cue is necessary and the patient recalls both name and address, score "0." If patient cannot spontaneously recall the name and address, cue with "John Brown" one time only. If this cue is necessary, the patient automatically has 2 errors. Score 1 point for each subsequent "unit" the participant cannot recall. The three units are: 42; Market Street; Chicago.
Concentration Test	
Items 23-25:	For uncorrected errors, score "2"; for self-corrected errors, score "1." For no errors, score "0." Indicate all errors and self corrections.

Source: Katzman R, Brown T, Fuld P, et al. Validation of a short orientation-memory-concentration test of cognitive impairment. Am J Psychiatry 1983;140:734-9. Copyright 1983, American Psychiatric Association. Used with permission.

4. A Short Test of Mental Status (STMS)

"I would now like to examine your memory and related items. Please relax, pay attention to the questions I am asking, and answer them as best as you can."

A Short Test of Mental Status (STMS)

1. Orientation (8)	Name, address, current location (building), city, state, date (day), month, year
2. Attention (7)	Digit span (present 1/sec; record longest correct span) 2-9-6-8-3, 5-7-1-9-4-6, 2-1-5-9-3-6-2
3. Immediate recall (4)	Four unrelated words: "apple," "Mr. Johnson," "charity," "tunnel." Number of trials needed to learn all four:
4. Calculation (4)	5 x 13; 65 - 7; 58/2; 29 + 11
5. Abstraction (3)	Similarities: orange/banana, dog/horse, table/bookcase
6. Construction (2)	Draw clock face showing 11:15
Copy (2)	
7. Information (4)	President; first President; define an island; number of weeks per year
8. Recall	The four words: "apple," "Mr. Johnson," "charity," "tunnel"

(4)	The four words: "apple," "Mr. Johnson," "charity," "tunnel"
Total Score: (38)	[Raw Score - (number of learning trials - 1)]

Instructions for Administration and Scoring of the Short Test of Mental Status (STMS)

Orientation

Each correct response is worth 1 point. The maximum score is 8.

Attention

Usually a span of five digits is given to the patient. If the patient responds correctly, the span is increased to six and then to seven. The patient's best performance is then recorded. If the patient is able to repeat seven digits forward, the test is terminated. The number of digits correctly repeated is the score; the maximal score is 7, and the minimal score is 0.

Immediate Recall

If the patient learns the words on the first trial, then the next subtest is given. If the patient is unable to learn all four words, the investigator repeats them for a maximum of 4 trials and records the number of trials that the patient requires to learn all 4 words. If the patient is unable to learn all four words by the end of the fourth trial, the patient's best performance is recorded (the number of words learned and the number of trials required). Learning is scored in two parts. A point is earned for each word learned (a maximum of 4 points). One less than the number of trials (a maximum of 4) required to learn the words was subtracted from the score. Thus, the values that were subtracted were between 0 and 3.

Calculation

Each correct answer earns 1 point, and the maximal score is 4.

Abstraction

One point for each word pair is given only for definitely abstract interpretations (for example, horse/dog = animal). Concrete interpretations or inability to see a similarity earns 0 points for that word pair. The maximal score is 3.

Construction and Copying

The patient is able to view the diagram of a cube while drawing his or her own version. For each construction, an adequate conceptual drawing is scored as 2, a less than complete drawing earns a score of 1, and inability to perform the task earns a score of 0. The maximum score for the construction tasks is 4.

Information

Each correct answer earns 1 point, and the maximal score is 4.

Recall

At the end of the test, the patient is asked to recall the four words from the immediate recall subtest. No cues or reminders are provided. The patient earns 1 point for each word recalled, and the maximal score is 4.

Total Score

Total score = sum of subtest scores minus (number of trials for acquisition minus 1). For example, if a patient learned all four words on the first trial, nothing was subtracted from the sum of the subtest scores. If a patient required four trials to learn some or all four words, then 3 was subtracted from the sum of the subtest scores.

Source: Kokmen E, Naessens JM, Offord KP. A short test of mental status: description and preliminary results. Mayo Clinic Proc 1987;62:281-8. Copyright 1987, Mayo Clinic Foundation. Used with permission.

References

Abranowicz M, editor. Drugs that cause psychiatric symptoms. *Med Lett Drugs Ther.* 1986; 28: 81–6. [PubMed]

Absher JR, Cummings JL. Dementia diagnosis and therapy in the elderly.

Compr Ther. 1992; 18: 28–33. [PubMed]

/Advisory Panel on Alzheimer's Disease. Fourth report of the Advisory Panel on Alzheimer's Disease, 1992 , Washington (DC):U.S. Government Printing Office; NIH Publication No. 93-3520 1993.

Albert MS, Heller HS, Milberg W. Changes in naming ability with age. *Psychol Aging.* 1988; 3: 173–8. [PubMed]

Albert MS, Levkoff SE, Reilly C, et al. The delirium symptoms interview: an interview for the detection of delirium symptoms in hospitalized patients *J Geriatr Psychiatry Neurol* 1992. 5: (1):14–21. [PubMed].

/Albert MS, Moss MB, editors. Geriatric neuropsychology , New York:Guilford Press;1988. –.

Alexopoulos GS, Abrams RC, Young RC, Shamoian CA. Cornell scale for depression in dementia. *Biol Psychiatry.* 1988; 23: 271–84. [PubMed]

/Alzheimer's Association. Is it Alzheimer's? Warning signs you should know , Chicago (IL):Alzheimer's Association;1995. . –.

Amaducci L, Falcini M, Lippi A. Descriptive epidemiology and risk factors for Alzheimer's disease *Acta Neurol Scand* 1992; . 139:(suppl):21–5.

American Academy of Neurology. Practice parameters for diagnosis and evaluation of dementia (summary statement): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology.* 1994; 44: 2203–6. [PubMed]

/American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed , Washington DC:American Psychiatric Association;1994.

Anthony JC, LeResche LA, Niaz U, et al. Limits of the "Mini-Mental State" as a screening test for dementia and delirium among hospital patients. *Psychol Med.* 1982; 12: 397–408. [PubMed]

Anthony JC, LeResche LA, Von Korff MR, et al. Screening for delirium on a general medical ward: the tachistoscope and a global accessibility rating. *Gen Hosp Psychiatry.* 1985; 7: 36–42. [PubMed]

Arenberg D. Misclassification of "probable senile dementia Alzheimer's type" in the Baltimore Longitudinal Study of Aging. *J Clin Epidemiol.* 1990; 43: 105–7. [PubMed]

Arendt G, Hefter H, Neuen-Jacob E, et al. Electropsychological motor testing, MRI findings and clinical course in AIDS patients with dementia. *J Neurol.* 1993; 240: 439–45. [PubMed]

Arnold SE, Kumar A. Reversible dementias. *Med Clin North Am.* 1993; 77: 215–30. [PubMed]

Bachman DL, Wolf PA, Linn RT, et al. Incidence of dementia and probable Alzheimer's disease in a general population: the Framingham Study. *Neurology.* 1993; 43: 515–9. [PubMed]

Barberger-Gateau P, Commenges D, Gagnon M, et al. Instrumental activities of daily living as a screening tool for cognitive impairment and dementia in elderly community dwellers. *J Am Geriatr Soc.* 1992; 40: 1129–34. [PubMed]

Barry PB, Moskowitz MA. The diagnosis of reversible dementia in the elderly: a critical review. *Arch Intern Med.* 1988; 148: 1914–8. [PubMed]

Bassett SS, Folstein MF. Cognitive impairment and functional disability in the absence of psychiatric diagnosis. *Psychol Med.* 1991; 21: 77–84. [PubMed]

Bayles KA, Kaszniak AW. Communication and cognition in normal aging and dementia ,

Boston:College-Hill/Little, Brown; 1987. –.

Bayles KA, Tomoeda CK. Caregiver report of prevalence and appearance order of linguistic symptoms in Alzheimer's patients. *Gerontologist.* 1991; 31: 210–6. [PubMed]

Becker JT, Bajulaiye O, Smith C. Longitudinal analysis of a two-component model of the memory deficit in Alzheimer's disease. *Psychol Med.* 1992; 22: 437–45. [PubMed]

/Benedict KB, Nacoste DB. Dementia and depression in the elderly: a framework for addressing difficulties in differential diagnosis. *Clin Psychol Rev.* 1990; 10: 513–37.

Berg L. Minor cognitive deficits and the detection of mild dementia *Psychiatr J Univ Ottawa* 1990. 15:(4):230–1.

Blazer D, Hughes DC, George LK. The epidemiology of depression in an elderly community population. *Gerontologist.* 1987; 27: 281–7. [PubMed]

Blazer D, Williams CD. Epidemiology of dysphoria and depression in an elderly population. *Am J Psychiatry.* 1980; 137: 439–44. [PubMed]

Bleecker ML, Bolla-Wilson K, Kawas C, Agnew J. Age-specific norms for the Mini-Mental State Exam. *Neurology.* 1988; 38: 1565–8. [PubMed]

Blessed G, Tomlinson BE, Roth M. The association between quantitative measures of dementia and of senile change in the cerebral grey matter of elderly subjects *Br J Psychiatry* 1968. 114:(512):797–811. [PubMed].

/Bondi MW, Kaszniak AW, Bayles KA, et al. Contributions of frontal system dysfunction to memory and perceptual abilities in Parkinson's disease. *Neuropsychology.* 1993; 7: 89–102.

Brayne C, Calloway P. The association of education and socioeconomic status with the Mini Mental State Examination and the clinical diagnosis of dementia in elderly people. *Age Ageing.* 1990; 19: 91–6. [PubMed]

Breitner JCS, Silverman JM, Mohs RC, et al. Familial aggregation in Alzheimer's disease: comparison of risk among relatives of early- and late-onset cases, and among male and female relatives in successive generations. *Neurology.* 1988; 38: 207–12. [PubMed]

Breitner JCS, Welsh KA. Diagnosis and management of memory loss and cognitive disorders among elderly persons. *Psychiatr Serv.* 1995; 46: 29–35. [PubMed]

Breteler MMB, Claus JJ, van Duijn CM, et al. Epidemiology of Alzheimer's disease. *Epidemiol Rev.* 1992; 14: 59–82. [PubMed]

/Brink TL, Yesavage JA, Lum O, et al. Screening tests for geriatric depression. *Clin Gerontologist.* 1982; 1: 37–43.

/Brust JCM. Neurological aspects of substance abuse , Boston: Butterworth-Heinemann; 1993. –.

Burke WJ, Rubin EH, Morris JC, et al. Symptoms of "depression" in dementia of the Alzheimer type. *Alzheimer Dis Assoc Disord.* 1988; 2: 356–62. [PubMed]

/Burns A. Affective symptoms in Alzheimer's disease. *Int J Geriatr Psychiatry.* 1991; 6: 371–6.

Burns A, Folstein S, Brandt J, et al. Clinical assessment of irritability, aggression, and apathy in Huntington and Alzheimer disease. *J Nerv Ment Dis.* 1990; 178: 20–6. [PubMed]

Burns A, Jacoby R, Levy R. Progression of cognitive impairment in Alzheimer's disease. *J Am Geriatr Soc.* 1991; 39: 39–45. [PubMed]

Burns A, Lewis G, Jacoby R, et al. Factors affecting survival in Alzheimer's disease. *Psychol Med.* 1991; 21: 363–70. [PubMed]

Butler RN, Finkel SI, Lewis MI, et al. Aging and mental health, part 2: diagnosis of dementia and depression. *Geriatrics.* 1992; 47: 49–52, 55-7. [PubMed]

/Caird FI, Scott PJW. Drug-induced disease in the elderly: a critical survey of the literature. Drug-induced disorders series Vol. 2:, Amsterdam: Elsevier Science;1986. . –.

Callahan CM, Hendrie HC, Tierney WM. Documentation and evaluation of cognitive impairment in elderly primary care patients. *Ann Intern Med.* 1995; 122: 422–9. [PubMed]

/Cedarbaum JM, Gancher ST, editors. Parkinson's disease. Neurologic clinics Vol. 10:, Philadelphia (PA): Saunders; 1992. . –.

Celesia GG, Wanamaker WM. Psychiatric disturbances in Parkinson's disease. *Dis Nerv Syst.* 1972; 33: 577–83. [PubMed]

Chatterjee A, Strauss ME, Smyth KA, et al. Personality changes in Alzheimer's disease. *Arch Neurol.* 1992; 49: 486–91. [PubMed]

Chaves MLF, Izquierdo I. Differential diagnosis between dementia and depression: a study of efficiency increment. *Acta Neurol Scand.* 1992; 85: 378–82. [PubMed]

/Clarfield AM. Canadian consensus conference on the assessment of dementia; 5-6 October 1989 , Montreal, Quebec:Canadian Consensus Conference on the Assessment of Dementia; 1991.

Clarfield AM. The reversible dementias: do they reverse? *Ann Intern Med.* 1988; 109: 476–86. [PubMed]

Cohen D, Eisdorfer C, Gorelick P, et al. Psychopathology associated with Alzheimer's disease and related disorders. *J Gerontol.* 1993; 48: M255–60. [PubMed]

Cohen-Mansfield J, Marx MS, Rosenthal AS. Dementia and agitation in nursing home residents: how are they related? *Psychol Aging.* 1990; 5: 3–8. [PubMed]

/Congress of the United States. Losing a million minds: confronting the tragedy of Alzheimer's disease and other dementias Congressional Summary, 1987. Report No. OTA-BA-32t , Washington, DC:Office of Technology Assessment;1989.

Corder EH, Saunders AM, Risch NJ, et al. Protective effect of apolipoprotein E type 2 allele for late onset Alzheimer disease. *Nat Genet.* 1994; 7: 180–3. [PubMed]

Corey-Bloom J, Galasko D, Hofstetter CR, et al. Clinical features distinguishing large cohorts with possible AD, probable AD, and mixed dementia. *J Am Geriatr Soc.* 1993; 41: 31–7. [PubMed]

/Costa PT Jr, McCrae RR. NEO-PI/NEO-FFI manual supplement , Odessa (FL): Psychological Assessment Resources;1989. –.

Cotrell V, Schulz R. The perspective of the patient with Alzheimer's disease: a neglected dimension of dementia research. *Gerontologist.* 1993; 33: 205–11. [PubMed]

/Cromwell SL. Antecedents and consequences of perceived memory adequacy in elders [dissertation] , Tucson (AZ):, University of Arizona; 1992.

Crook TH, West RL. Name recall performance across the adult life-span. *Br J Psychol.* 1990; 81: 335–49. [PubMed]

Crum RM, Anthony JC, Bassett SS, et al. Population-based norms for the Mini-Mental State Examination by age and educational level. *JAMA.* 1993; 269: 2386–91. [PubMed]

/Cummings JL, Benson DF. Dementia: a clinical approach 2nd ed , Boston: Butterworth-Heinemann; 1992. –.

/Davis K, Neuman P. Financing care for patients with Alzheimer's disease and related disorders. Prepared for the Office of Technology Assessment Workshop on Financing Care for Patients With Alzheimer's Disease and Related Disorders. Economics, Social Science and Health Services Research, Dementia Working Papers Vol. 2:, Springfield (VA):National Technical Information Service; 1986. –.

/Delis DC, Massman PJ, Butters N, et al. Profiles of demented and amnesic patients on the California Verbal Learning Test: implications for the assessment of memory disorders. *Psychol Assess: J Consult Clin Psychol.* 1991; 3: 19–26.

Deutch LH, Deutsch LH, Rovner BW. Agitation and other noncognitive abnormalities in Alzheimer's disease. *Psychiatr Clin North Am.* 1991; 14: 341–51. [PubMed]

Devanand DP, Miller L, Richards M, et al. The Columbia University Scale for Psychopathology in Alzheimer's Disease. *Arch Neurol.* 1992; 49: 371–6. [PubMed]

Differential diagnosis of dementing diseases. NIH Consensus Statement 1987 July 6-8. 6(11):1-9.

Duchek JM, Cheney M, Ferraro FR, et al. Paired associate learning in senile dementia of the Alzheimer type. *Arch Neurol.* 1991; 48: 1038–40. [PubMed]

Erkinjuntti T, Wikström J, Palo J, et al. Dementia among medical inpatients: evaluation of 2000 consecutive admissions. *Arch Intern Med.* 1986; 146: 1923–6. [PubMed]

Ernst RL, Hay JW. The US economic and social costs of Alzheimer's disease revisited. *Am J Public Health.* 1994; 84: 1261–4. [PubMed] [Free Full text in PMC]

Escobar JI, Burnam A, Karno M, et al. Use of the Mini-Mental Status Examination (MMSE) in a community population of mixed ethnicity: cultural and linguistic artifacts. *J Nerv Ment Dis.* 1986; 174: 607–14. [PubMed]

Evans DA, Funkenstein HH, Albert MS, et al. Prevalence of Alzheimer's disease in a community population of older persons: higher than previously reported. *JAMA.* 1989; 262: 2551–6. [PubMed]

Evans DA, Scherr PA, Cook NR, et al. Estimated prevalence of Alzheimer's disease in the United States. *Milbank Q.* 1990; 68: 267–89. [PubMed]

Feher EP, Larrabee GJ, Crook TH III. Factors attenuating the validity of the Geriatric Depression Scale in a dementia population. *J Am Geriatr Soc.* 1992; 40: 906–9. [PubMed]

Flicker C. Neuropsychological evaluation of treatment effects in the elderly: a critique of tests in current use. *Psychopharmacol Bull.* 1988; 24: 535–56. [PubMed]

Flicker C, Ferris SH, Reisberg B. Mild cognitive impairment in the elderly: predictors of dementia. *Neurology.* 1991; 41: 1006–9. [PubMed]

Folstein MF, Bassett SS, Anthony JC, et al. Dementia: case ascertainment in a community survey. *J Gerontol.* 1991; 46: M132–8. [PubMed]

Folstein MF, Folstein SE, McHugh PR. "Mini-Mental State": a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* 1975; 12: 189–98. [PubMed]

Fratiglioni L, Grut M, Forsell Y, et al. Prevalence of Alzheimer's disease and other dementias in an elderly urban population: relationship with age, sex, and education. *Neurology.* 1991; 41: 1886–92. [PubMed]

/Fry PS. Depression, stress, and adaptations in the elderly: psychological assessment and intervention , Rockville (MD):Aspen; 1986. –.

/Fuld PA. The Fuld Object-Memory Evaluation , Chicago:Stoelting Instrument Co.; 1981.

/Gallagher D. Assessment of depression by interview methods and psychiatric rating scales. In: Poon LW, editor. Handbook for clinical memory assessment in older adults , Washington (DC):American Psychological Association; 1986. . p. 202–12.

Ganguli M, Ratcliff G, Huff FJ, et al. Effects of age, gender, and education on cognitive tests in a rural elderly community sample: norms from the Monongahela Valley Independent Elders Survey. *Neuroepidemiology.* 1991; 10: 42–52. [PubMed]

Garcia CA, Reding MJ, Blass JP. Overdiagnosis of dementia.
J Am Geriatr Soc. 1981; 29: 407–10. [PubMed]

German PS, Shapiro S, Skinner EA, et al. Detection and management of mental health problems of older patients by primary care providers. *JAMA.* 1987; 257: 489–93. [PubMed]

Gottlieb GL, Johnson J, Wanich C, et al. Delirium in the medically ill elderly: operationalizing the DSM-III criteria. *Int Psychogeriatr.* 1991; 3: 181–96. [PubMed]

Grafman J, Weingartner H, Newhouse PA, et al. Implicit learning in patients with Alzheimer's disease. *Pharmacopsychiatry.* 1990; 23: 94–101. [PubMed]

/Grant I, Adams KM, editors. Neuropsychological assessment of neuropsychiatric disorders , New York: Oxford University Press; 1986. . –.

Graves AB, White E, Koepsell TD, et al. A case-control study of Alzheimer's disease. *Ann Neurol.* 1990; 28: 766–74. [PubMed]

Green CR, Mohs RC, Schmeidler J, et al. Functional decline in Alzheimer's disease: a longitudinal study. *J Am Geriatr Soc.* 1993; 41: 654–61. [PubMed]

Greene MG, Majerovitz SD, Adelman RD, et al. The effects of the presence of a third person on the physician-older patient medical interview.
J Am Geriatr Soc. 1994; 42: 413–9. [PubMed]

Grut M, Jorm AF, Fratiglioni L, et al. Memory complaints of elderly people in a population survey: variation according to dementia stage and depression.
J Am Geriatr Soc. 1993; 41: 1295–1300. [PubMed]

/Gurland BJ, Cross P, Chen J, et al. A new performance test of adaptive cognitive functioning: the medication management (MM) test.
Int J Geriatr Psychiatry. 1994; 9: 875–85.

/Gurland BJ, Wilder DE, Chen J, et al. A flexible system of detection for Alzheimer's disease and related dementias. *Aging Clin Exp Res.* 1995; 7: 165–72.

/Gurland BJ, Wilder DE, Cross P, et al. Relative rates of dementia by multiple case definitions over two prevalence periods in three sociocultural groups.
Am J Geriatr Psychiatry. 1995; 3: 6–20.

Harris MJ, Gierz M, Lohr JB. Recognition and treatment of depression in Alzheimer's disease. *Geriatrics.* 1989; 44: 26–30. [PubMed]

Hart S. Language and dementia: a review. *Psychol Med.* 1988; 18: 99–112. [PubMed]

Hasselblad V, Hedges LV. Meta-analysis of screening and diagnostic tests.
Psychol Bull. 1995; 117: 167–78. [PubMed]

Hay JW, Ernst RL. The economic costs of Alzheimer's disease.
Am J Public Health. 1987; 77: 1169–75. [PubMed] [Free Full text in PMC]

/Heaton RK, Grant I, Matthews CG. Differences in neuropsychological test performance

associated with age, education, and sex. In: Grant I, Adams KM, editors. Neuropsychological assessment of neuropsychiatric disorders New York, Oxford University Press; 1986. p. 100–20.

Heaton RK, Pendleton MG. Use of neuropsychological tests to predict adult patients' everyday functioning. *J Consult Clin Psychol.* 1981; 49: 807–21. [PubMed]

/Hedges LV, Okin I. Statistical methods for meta-analysis. *San Diego (CA): Academic Press.* 1985: –.

Heller RB, Dobbs AR, Rule BG. Communicative function in patients with questionable Alzheimer's disease. *Psychol Aging.* 1992; 7: 395–400. [PubMed]

/Henderson AS. Epidemiology of dementia disorders. In: Wurtman RJ, Corkin S, Growdon JH, Ritter-Walker E, editors. Advances in neurology. Vol. 51: Alzheimer's disease , New York:Raven Press;1990. . p. 15–25.

Henderson AS, Huppert FA. The problem of mild dementia [editorial]. *Psychol Med.* 1984; 14: 5–11. [PubMed]

Henderson VW, Mack W, Williams BW. Spatial disorientation in Alzheimer's disease. *Arch Neurol.* 1989; 46: 391–4. [PubMed]

Hershey LA, Jaffe DF, Greenough PG, et al. Validation of cognitive and functional assessment instruments in vascular dementia. *Int J Psychiatry Med.* 1987; 17: 183–92. [PubMed]

Heyman A, Fillenbaum G, Prosnitz B, et al. Estimated prevalence of dementia among elderly black and white community residents. *Arch Neurol.* 1991; 48: 594–8. [PubMed]

Hof PR, Bouras C, Constantinidis J, et al. Selective disconnection of specific visual association pathways in cases of Alzheimer's disease presenting with Balint's syndrome. *J Neuropathol Exp Neurol.* 1990; 49: 168–84. [PubMed]

Hoffman RS. Diagnostic errors in the evaluation of behavioral disorders. *JAMA.* 1982; 248: 964–7. [PubMed]

Howieson DB, Holm LA, Kaye JA, et al. Neurologic function in the optimally healthy oldest old: neuropsychological evaluation. *Neurology.* 1993; 43: 1882–6. [PubMed]

Hu TW, Huang LF, Cartwright WS. Evaluation of the costs of caring for the senile demented elderly: a pilot study. *Gerontologist.* 1986; 26: 158–63. [PubMed]

Huang LF, Cartwright WS, Hu TW. The economic cost of senile dementia in the United States, 1985. *Public Health Rep.* 1988; 103: 3–7. [PubMed]

Hultsch DF, Hertzog C, Small BJ, et al. Short-term longitudinal change in cognitive performance in later life. *Psychol Aging.* 1992; 7: 571–84. [PubMed]

Hyman BT, West HL, Rebeck GW, et al. Quantitative analysis of senile plaques in Alzheimer's disease: observation of log-normal size distribution and particular molecular epidemiology of differences associated with APOE genotypes and trisomy 21 Down syndrome. *Proc Natl Acad Sci U S A.* 1995; 92: 3586–90. [PubMed] [Free Full text in PMC]

Inouye SK, van Dyck CH, Alessi CA, et al. Clarifying confusion: the Confusion Assessment Methoda new method for detection of delirium. *Ann Intern Med.* 1990; 113: 941–8. [PubMed]

Inouye SK, Viscoli CM, Horwitz RI, et al. A predictive model for delirium in hospitalized elderly medical patients based on admission characteristics. *Ann Intern Med.* 1993; 119: 474–81. [PubMed]

Johnson JC, Kerse NM, Gottlieb G, et al. Prospective versus retrospective methods of identifying patients with delirium. *J Am Geriatr Soc.* 1992; 40: 316–9. [PubMed]

/Jorm AF. The epidemiology of Alzheimer's disease and related disorders , London: Chapman & Hall;1990. . –.

Jorm AF, Korten AE. Assessment of cognitive decline in the elderly by informant interview. *Br J Psychiatry.* 1988; 152: 209–13. [PubMed]

/Kaeming KL, Kaszniak AW. Neuropsychological aspects of human immunodeficiency virus infection. *Clin Neuropsychol.* 1989; 3: 309–26.

Kahn RL, Zarit SH, Hilbert NM, et al. Memory complaint and impairment in the aged: the effect of depression and altered brain function.
Arch Gen Psychiatry. 1975; 32: 1569–73. [PubMed]

/Kaszniak AW, Allender J. Psychological assessment of depression in older adults. In: Chaisson-Stewart GM, editor. Depression in the elderly: an interdisciplinary approach , New York:Wiley; 1985. . p. 107–60.

Kaszniak AW, Fox J, Gandell DL, et al. Predictors of mortality in presenile and senile dementia. *Ann Neurol.* 1978; 3: 246–52. [PubMed]

Kaszniak AW, Keyl PM, Albert MS. Dementia and the older driver.
Hum Factors. 1991; 33: 527–37. [PubMed]

/Kaszniak AW, Sadeh M, Stern LZ. Differentiating depression from organic brain syndromes in older age. In: Chaisson-Stewart GM, editor. Depression in the elderly: an interdisciplinary approach , New York: Wiley; 1985. . p. 161–89.

Kaszniak AW, Wilson RS, Fox JH, et al. Cognitive assessment in Alzheimer's disease: cross-sectional and longitudinal perspectives. *Can J Neurol Sci.* 1986; 13: 420–3. [PubMed]

/Katz S, Ford AB, Moskowitz RW, et al. Studies of illness in the aged. The index of ADL: a standardized measure of biological and psychosocial function.
JAMA. 1963; 185: 914–9. [PubMed]

Katzman R, Brown T, Fuld P, et al. Validation of a short orientation-memory-concentration test of cognitive impairment. *Am J Psychiatry.* 1983; 140: 734–9. [PubMed]

/Katzman R, Lasker B, Bernstein N. Advances in the diagnosis of dementia: accuracy of diagnosis and consequences of misdiagnosis of disorders causing dementia. In: Terry RD, editor. Aging and the brain , New York:Raven Press; 1988. . p. 17–62.

/Katzman R, Rowe JW, editors. Principles of geriatric neurology , Philadelphia: FA Davis; 1992. . –.

/Katzman R, Terry RD, Bick KL, editors. Alzheimer's disease: senile dementia and related disorders. Aging series. Vol. 7 , New York:Raven;1978. –.

Kemper S, LaBarge E, Ferraro FR, et al. On the preservation of syntax in Alzheimer's disease: evidence from written sentences. *Arch Neurol.* 1993; 50: 81–6. [PubMed]

Khachaturian ZS. Diagnosis of Alzheimer's disease. *Arch Neurol.* 1985; 42: 1097–105. [PubMed]

/Kiloh LG. Pseudo-dementia. *Acta Psychiatr Scand.* 1961; 37: 336–51. [PubMed]

/Klerman GL. Problems in the definition and diagnosis of depression in the elderly. In: Breslau LD, Haug MR, editors. Depression and aging: causes, care and consequences , New York:Springer; 1983. p. 3–19.

Knopman D. Long-term retention of implicitly acquired learning in patients with Alzheimer's disease. *J Clin Exp Neuropsychol.* 1991; 13: 880–94. [PubMed]

Knopman DS, Ryberg S. A verbal memory test with high predictive accuracy for dementia of the Alzheimer type. *Arch Neurol.* 1989; 46: 141–5. [PubMed]

/Koenig HG, Blazer DG. Mood disorders and suicide. In: Birren JE, Sloane RB, Cohen GD, et al., editors. Handbook of mental health and aging. 2nd ed , San Diego: Academic Press;1992. p. 379–407.

Kokmen E, Naessens JM, Offord KP. A Short Test of Mental Status: description and preliminary results. *Mayo Clin Proc.* 1987; 62: 281–8. [PubMed]

/Kolb B, Whishaw IQ. Fundamentals of human neuropsychology. 3rd ed , New York: WH Freeman; 1990. . –.

/Koskinen T. Pseudodementia as a manifestation of depression in the elderly. *Psychiatr Fenn.* 1992; 23: 123–9.

/LaBarge E, Balota DA, Storandt M, et al. An analysis of confrontation naming errors in senile dementia of the Alzheimer type. *Neuropsychology.* 1992; 6: 77–95.

/LaBarge E, Rosenman LS, Leavitt K, et al. Counseling clients with mild senile dementia of the Alzheimer's type: a pilot study. *J Neurol Rehab.* 1988; 2: 167–73.

LaBarge E, Smith DS, Dick L, et al. Agraphia in dementia of the Alzheimer type. *Arch Neurol.* 1992; 49: 1151–6. [PubMed]

/Lanska DJ, Schoenberg BS. The epidemiology of dementia: methodologic issues and approaches. In: Whitehouse PJ, editor. Dementia , Philadelphia (PA):FA Davis; 1993. . p. 3–33.

Larrabee GL, Levin HS. Memory self-ratings and objective test performance in a normal elderly sample. *J Clin Exp Neuropsychol.* 1986; 8: 275–84. [PubMed]

Larson EB, Kukull WA, Buchner D, et al. Adverse drug reactions associated with global cognitive impairment in elderly persons. *Ann Intern Med.* 1987; 107: 169–73. [PubMed]

Larson EB, Reifler BV, Featherstone HJ, et al. Dementia in elderly outpatients: a prospective study. *Ann Intern Med.* 1984; 100: 417–23. [PubMed]

Larson EB, Reifler BV, Sumi SM, et al. Diagnostic evaluation of 200 elderly outpatients with suspected dementia. *J Gerontol.* 1985; 40: 536–43. [PubMed]

Larson EB, Reifler BV, Sumi SM, et al. Diagnostic tests in the evaluation of dementia: a prospective study of 200 elderly patients. *Arch Intern Med.* 1986; 146: 1917–22. [PubMed]

/La Rue A. Aging and neuropsychological assessment , New York: Plenum; 1992. . –.

La Rue A, Watson J, Plotkin DA. Retrospective accounts of dementia symptoms: are they reliable? *Gerontologist.* 1992; 32: 240–5. [PubMed]

/La Rue A, Yang J, Osato S. Neuropsychological assessment. In: Birren JE, Sloane RB, Cohen GD, editors. Handbook of mental health and aging 2nd ed , San Diego (CA):Academic Press;1992. p. 643–70.

Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist.* 1969; 9: 179–86. [PubMed]

Lazarus LW, Newton N, Cohler B, et al. Frequency and presentation of depressive symptoms in patients with primary degenerative dementia. *Am J Psychiatry.* 1987; 144: 41–5. [PubMed]

/Lesher EL. Validation of the Geriatric Depression Scale among nursing home residents. *Clin Gerontol.* 1986; 4: 21–8.

Levkoff S, Cleary P, Liptzin B, et al. Epidemiology of delirium: an overview of research issues and findings. *Int Psychogeriatr.* 1991; 3: 149–67. [PubMed]

Levkoff SE, Evans DA, Liptzin B, et al. Delirium: the occurrence and persistence of symptoms among elderly hospitalized patients. *Arch Intern Med.* 1992; 152: 334–40. [PubMed]

Levy-Lahad E, Wijsman EM, Nemens E, et al. A familial Alzheimer's disease locus on chromosome 1. *Science.* 1995; 269: 970–2. [PubMed]

/Lezak MD. Neuropsychological assessment. 3rd ed , New York: Oxford University Press; 1995. –.

/Lipowski ZJ. Delirium: acute brain failure in man. 2nd ed , New York: Oxford University Press;1990. . –.

/Loewenstein DA. Objective assessment of functional status in Alzheimer's disease and related disorders. *Clin Gerontol.* 1990; 10: 61–4.

/Loewenstein DA, Argüelles T, Barker WW, et al. A comparative analysis of neuropsychological test performance of Spanish-speaking and English-speaking patients with Alzheimer's disease. *J Gerontol.* 1993; 48: 142–9.

/Logie SA, Murphy JB, Brooks DN, et al. Diagnosis of depression in patients with dementia: use of the Cambridge Mental Disorders of the Elderly Examination (CAMDEX). *Int J Geriatr Psychiatry.* 1992; 7: 363–8.

/Lopez SR, Taussig IM. Cognitive-intellectual functioning of Spanish-speaking impaired and nonimpaired elderly; implications for culturally sensitive assessment. *Psychol Assess.* 1991; 3: 448–54.

Mackenzie TB, Robiner WN, Knopman DS. Differences between patient and family assessments of depression in Alzheimer's disease. *Am J Psychiatry.* 1989; 146: 1174–8. [PubMed]

Mahurin RK, DeBettignies BH, Pirozzolo FJ. Structured assessment of independent living skills: preliminary report of a performance measure of functional abilities in dementia. *J Gerontol.* 1991; 46: 58–66.

Mant A, Eyland EA, Pond DC, et al. Recognition of dementia in general practice: comparison of general practitioners' opinions with assessments using the Mini-Mental State Examination and the Blessed Dementia Rating Scale. *Fam Pract.* 1988; 5: 184–8. [PubMed]

McCartney JR, Palmateer LM. Assessment of cognitive deficit in geriatric patients: a study of physician behavior. *J Am Geriatr Soc.* 1985; 33: 467–71. [PubMed]

/McGlynn SM, Kaszniak AW. When metacognition fails: impaired awareness of deficit in Alzheimer's disease. *J Cogn Neurosci.* 1991; 3: 183–9.

McIntyre L, Frank J. Evaluation of the demented patient. *J Fam Prac.* 1987; 24: 399–404.

McKhann G, Drachman D, Folstein M, et al. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology.* 1984; 34: 939–44. [PubMed]

Mendez MF, Mendez MA, Martin R, et al. Complex visual disturbances in Alzheimer's disease. *Neurology.* 1990; 40: 439–43. [PubMed]

Merriam AE, Aronson MK, Gaston P, et al. The psychiatric symptoms of Alzheimer's disease. *J Am Geriatr Soc.* 1988; 36: 7–12. [PubMed]

/Miller NE. The measurement of mood in senile brain disease: examiner ratings and

self-reports. In: Cole JO, Barrett JE, editors. Psychopathology in the aged , New York: Raven Press;1980 . p. 97–118.

Mitrushina M, Satz P. Utility of Mini-Mental State Examination in assessing cognition in the elderly. *Aging.* 1994; 6: 427–32. [PubMed]

Mohs RC, Breitner JCS, Silverman JM, et al. Alzheimer's disease: morbid risk among first-degree relatives approximates 50% by 90 years of age.
Arch Gen Psychiatry. 1987; 44: 405–8. [PubMed]

Morris JC. Differential diagnosis of Alzheimer's disease.
Clin Geriatr Med. 1994; 10: 257–76. [PubMed]

Morris JC, McKeel DW Jr, Storandt M, et al. Very mild Alzheimer's disease: informant-based clinical, psychometric, and pathologic distinction from normal aging.
Neurology. 1991; 41: 469–78. [PubMed]

Morrison RL, Katz IR. Drug-related cognitive impairment: current progress and recurrent problems. *Annu Rev Gerontol Geriatr.* 1989; 9: 232–79. [PubMed]

/Mortimer JA. What are the risk factors for dementia? In: Huppert FA, Brayne C, O'Connor DW, editors. Dementia and normal aging , Cambridge (UK):Cambridge University Press;1994. . p. 208–29.

/Mortimer JA, Graves AB. Education and other socioeconomic determinants of dementia and Alzheimer's disease *Neurology* 1993. 43:(suppl 4):S39–S44. [PubMed].

/Mortimer JA, Hutton JT. Epidemiology and etiology of Alzheimer's disease. In: Hutton JT, Kenny AD, editors. Senile dementia of the Alzheimer type. Neurology and neurobiology Vol. 18:, New York: Alan R. Liss; 1985. . p. 177–96.

Mortimer JA, van Duijn CM, Chandra V, et al. Head trauma as a risk factor for Alzheimer's disease: a collaborative re-analysis of case-control studies *Int J Epidemiol* 1991. 20:(suppl 2):S28–S35. [PubMed].

Murden RA, McRae TD, Kaner S, et al. Mini-Mental State Exam scores vary with education in blacks and whites. *J Am Geriatr Soc.* 1991; 39: 149–55. [PubMed]

Nathan BP, Bellosta S, Sanan DA, et al. Differential effects of apolipoproteins E3 and E4 on neuronal growth in vitro. *Science.* 1994; 264: 850–2. [PubMed]

/National Institute on Aging. Alzheimer's disease costs the nation an estimated 90 billion dollars per year: progress report on Alzheimer's disease , Bethesda (MD): National Institute on Aging; 1993. –.NIH Publication No. 93-3409 (Discoveries in Health for Aging Americans series) .

National Institutes of Health. Consensus Development Panel on Depression in Late Life. Diagnosis and treatment of depression in late life. *JAMA.* 1992; 268: 1018–24. [PubMed]

/Naugle RI, Cullum CM, Bigler ED. Evaluation of intellectual and memory function among dementia patients who were intellectually superior.
Clin Neuropsychol. 1990; 4: 355–74.

Nebes RD. Semantic memory in Alzheimer's disease. *Psychol Bull.* 1989; 106: 377–94. [PubMed]

Nebes RD, Brody CP. Integrity of semantic fields in Alzheimer's disease.
Cortex. 1988; 24: 291–9. [PubMed]

Nebes RD, Norton DC, Horn LL. Sparing of semantic memory in Alzheimer's disease.
J Abnormal Psychol. 1984; 93: 321–30.

Nelson A, Fogel BS, Faust D. Bedside cognitive screening instruments: a critical assessment. *J Nerv Ment Dis.* 1986; 174: 73–83. [PubMed]

Nelson HE, O'Connell A. Dementia: the estimation of premorbid intelligence levels using the New Adult Reading Test. *Cortex.* 1978; 14: 234–44. [PubMed]

Nierenberg AA, Feinstein AR. How to evaluate diagnostic marker tests. Lessons from the rise and fall of dexamethasone suppression test *JAMA* 1988. 259:(11):1699–1702. [PubMed].

O'Brien ME. The dementia syndromes: distinguishing their clinical differences. *Postgrad Med.* 1994; 95: 91–3, 97-9, 101. [PubMed]

O'Connor DW, Fertig A, Grande MJ, et al. Dementia in general practice: the practical consequences of a more positive approach to diagnosis. *Br J Gen Pract.* 1993; 43: 185–8. [PubMed] [Free Full text in PMC]

O'Connor DW, Pollitt PA, Hyde JB, et al. Do general practitioners miss dementia in elderly patients? *Br Med J.* 1988; 297: 1107–10. [PubMed] [Free Full text in PMC]

O'Connor DW, Pollitt PA, Hyde JB, et al. The reliability and validity of the Mini-Mental State in a British community survey. *J Psychiatr Res.* 1989; 23: 87–96. [PubMed]

O'Connor DW, Pollitt PA, Hyde JB, et al. Clinical issues relating to the diagnosis of mild dementia in a British community survey. *Arch Neurol.* 1991; 48: 530–4. [PubMed]

/Parks RW, Zec RF, Wilson RS, editors. Neuropsychology of Alzheimer's disease and other dementias , New York: Oxford University Press; 1993. –.

Parmelee PA, Katz IR, Lawton MP. Depression among institutionalized aged: assessment and prevalence estimation. *J Gerontol.* 1989; 44: M22–9. [PubMed]

Paveza GJ, Cohen D, Eisdorfer C, et al. Severe family violence and Alzheimer's disease: prevalence and risk factors. *Gerontologist.* 1992; 32: 493–7. [PubMed]

Perls TT. The oldest old *Sci Am* 1995. 272:(1):70–5. [PubMed].

Peters CA, Potter JF, Scholer SG. Hearing impairment as a predictor of cognitive decline in dementia. *J Am Geriatr Soc.* 1988; 36: 981–6. [PubMed]

Petry S, Cummings JL, Hill MA, et al. Personality alterations in dementia of the Alzheimer type. *Arch Neurol.* 1988; 45: 1187–90. [PubMed]

Petry S, Cummings JL, Hill MA, et al. Personality alterations in dementia of the Alzheimer type: a three-year follow-up study. *J Geriatr Psychiatry Neurol.* 1989; 2: 203–7. [PubMed]

/Pfeffer RI. A social function measure in the staging and study of dementia. In: Bergener M, Brocklehurst JC, Finkel SI, editors. Aging, health, and healing , New York:Springer; 1995. . –.

Pfeffer RI, Kurosaki TT, Harrah CH, et al. Measurement of functional activities in older adults in the community. *J Gerontol.* 1982; 37: 323–9. [PubMed]

Philbrick JT, Horwitz RI, Feinstein AR. Methodologic problems of exercise testing for coronary artery disease: groups, analysis and bias. *Am J Cardiol.* 1980; 46: 807–12. [PubMed]

Pinholt EM, Kroenke K, Hanley JF, et al. Functional assessment of the elderly: a comparison of standard instruments with clinical judgment. *Arch Intern Med.* 1987; 147: 484–8. [PubMed]

Plude DJ, Milberg WP, Cerella J. Age differences in depicting and perceiving tridimensionality in simple line drawings. *Exp Aging Res.* 1986; 12: 221–5. [PubMed]

Poirier J, Davignon J, Bouthillier D, et al. Apolipoprotein E polymorphism and Alzheimer's disease. *Lancet.* 1993; 342: 697–9. [PubMed]

/Pollitt PA, O'Connor DW, Anderson L. Mild dementia: perceptions and problems. *Ageing Soc.* 1989; 9: 261–75.

Popkin MK, Tucker GJ. "Secondary" and drug-induced mood, anxiety, psychotic, catatonic, and personality disorders: a review of the literature. *J Neuropsychiatry Clin Neurosci.* 1992; 4: 369–85. [PubMed]

/Rabins PV. Does reversible dementia exist and is it reversible? [editorial]. *Arch Intern Med.* 1988; 148: –.

Rabins PV, Mace NL, Lucas MJ. The impact of dementia on the family. *JAMA.* 1982; 248: 333–5. [PubMed]

Ransohoff DF, Feinstein AR. Problems of spectrum and bias in evaluating the efficacy of diagnostic tests. *N Engl J Med.* 1978; 299: 926–30. [PubMed]

/Raskind MA, Peskind ER. Alzheimer's disease and other dementing disorders. In: Birren JE, Sloane RB, Cohen GD, editors. Handbook of mental health and aging. 2nd ed , San Diego (CA):Academic Press; 1992. . p. 477–513.

Reding M, Haycox J, Blass J. Depression in patients referred to a dementia clinic: a three-year prospective study. *Arch Neurol.* 1985; 42: 894–6. [PubMed]

Reifler BV, Larson E, Hanley R. Coexistence of cognitive impairment and depression in geriatric outpatients. *Am J Psychiatry.* 1982; 139: 623–6. [PubMed]

Reisberg B, Ferris SH, Franssen E. An ordinal functional assessment tool for Alzheimer's-type dementia. *Hosp Community Psychiatry.* 1985; 36: 593–5. [PubMed]

/Reisberg B, Franssen E, Sclan SG, et al. Stage specific incidence of potentially remediable behavioral symptoms in aging and Alzheimer disease. *Bull Clin Neurosci.* 1989; 54: 95–112.

Rice DP, Fox PJ, Max W, et al. The economic burden of Alzheimer's disease care. *Health Aff (Millwood).* 1993; 12: 164–76. [PubMed]

/Rice DP, Max W. Costs of aging-related illnesses: a synthesis of current studies. Final report to the Office of Demography of Aging National Institute on Aging,1993. –.

Roca RP, Klein LE, Kirby SM, et al. Recognition of dementia among medical patients. *Arch Intern Med.* 1984; 144: 73–5. [PubMed]

Roses AD, Strittmatter WJ, Pericak-Vance MA, et al. Clinical application of apolipoprotein E genotyping to Alzheimer's disease [letter]. *Lancet.* 1994; 343: 1564–5. [PubMed]

Roth ME. Advances in Alzheimer's disease. A review for the family physician. *J Fam Pract.* 1993; 37: 593–607. [PubMed]

Rovner BW, German PS, Broadhead J, et al. The prevalence and management of dementia and other psychiatric disorders in nursing homes. *Int Psychogeriatr.* 1990; 2: 13–24. [PubMed]

Royston ML, Mann D, Pickering-Brown S, et al. APOE 2 allele promotes longevity and protects patients with Down Syndrome from dementia. *Neuroreport.* 1994; 5: 2583–5. [PubMed]

/Rubin EH. Psychopathology of senile dementia of the Alzheimer type. In: Wurtman RJ, Corkin S, Growdon JH, Ritter-Walker E, editors. Advances in neurology, Vol. 51. Alzheimer's disease , New York: Raven Press; 1990. . p. 53–9.

Rubin EH, Kinscherf DA. Psychopathology of very mild dementia of the Alzheimer type. *Am J Psychiatry.* 1989; 146: 1017–21. [PubMed]

Rubin EH, Morris JC, Berg L. The progression of personality changes in senile dementia of the Alzheimer's type. *J Am Geriatr Soc.* 1987; 35: 721–5. [PubMed]

Rubin EH, Morris JC, Storandt M, et al. Behavioral changes in patients with mild senile dementia of the Alzheimer's type. *Psychiatry Res.* 1987; 21: 55–62. [PubMed]

Rubin EH, Zorumski CF, Burke WJ. Overlapping symptoms of geriatric depression and Alzheimer-type dementia. *Hosp Community Psychiatry.* 1988; 39: 1074–9. [PubMed]

Rubin SM, Glasser ML, Werckle MA. The examination of physicians' awareness of dementing disorders. *J Am Geriatr Soc.* 1987; 35: 1051–8. [PubMed]

Rush JA, Golden WE, Hall GW, et al. Depression in primary care: Volume I. Detection and diagnosis. Clinical Practice Guideline No. 5. AHCPR Publication No. 93-0550 , Rockville (MD): Agency for Health Care Policy and Research, Public Health Service, U.S. Department of Health and Human Services.April 1993.

/Salzman C, editor. Clinical geriatric psychopharmacology. 2nd ed , Baltimore: Williams & Wilkins; 1992. . –.

Sapir M. Re: Prevalence of Alzheimer's disease in a retirement community [letter]. *Am J Epidemiol.* 1988; 127: 1093–5. [PubMed]

Saunders AM, Schmader K, Breitner JCS, et al. Apolipoprotein E[epsilon] 4 allele distribution in late-onset Alzheimer's disease and in other amyloid-forming diseases. *Lancet.* 1993; 342: 710–1. [PubMed]

/Schaie KW. The optimization of cognitive functioning in old age: predictions based on cohort-sequential and longitudinal data. In: Baltes PB, Baltes MM, editors. Successful aging: perspectives from the behavioral sciences , Cambridge (MA): Cambridge University Press; 1990. p. 94–117.

Schellenberg GD, Bird TD, Wijsman EM, et al. Genetic linkage evidence for a familial Alzheimer's disease locus on chromosome 14. *Science.* 1992; 258: 668–71. [PubMed]

Schoenberg BS, Anderson DW, Haerer AF. Severe dementia: prevalence and clinical features in a biracial US population. *Arch Neurol.* 1985; 42: 740–3. [PubMed]

/Scogin F. The concurrent validity of the Geriatric Depression Scale with depressed older adults. *Clin Gerontol.* 1987; 7: 23–31.

Sherrington R, Rogaev EI, Liang Y, et al. Cloning of a gene bearing missense mutations in early-onset familial Alzheimer's disease. *Nature.* 1995; 375: 754–60. [PubMed]

/Siegel B, Gershon S. Dementia, depression, and pseudodementia. In: Altman HJ, editor. Alzheimer's disease: problems, prospects, and perspectives , New York: Plenum;1986. . p. 29–44.

/Siegler IC, Poon LW, Madden DJ. Psychological aspects of normal aging. In: Busse E, Blazer DG, editors. The American Psychiatric Press textbook of geriatric psychiatry. 2nd ed , Washington (DC):American Psychiatric Press; 1995. p. 113–39.

Siegler IC, Welsh KA, Dawson DV, et al. Ratings of personality change in patients being evaluated for memory disorders. *Alzheimer Dis Assoc Disord.* 1991; 5: 240–50. [PubMed]

Siu AL. Screening for dementia and investigating its causes. *Ann Intern Med.* 1991; 115: 122–32. [PubMed]

Skoog I, Nilsson L, Palmertz B, et al. A population-based study of dementia in 85-year-olds. *N Engl J Med.* 1993; 328: 153–8. [PubMed]

Small GW, Jarvik LF. The dementia syndrome. *Lancet.* 1982: 1443–6. [PubMed]

/Smith CW, Byrne EJ, Arie T, et al. Diagnosis of dementia. II-diagnostic methods: a

survey of current consultant practice and review of the literature.
Int J Geriatr Psychiatry. 1992; 7: 323–9.

Smith JS, Kiloh LG. The investigation of dementia: results in 200 consecutive admissions. *Lancet.* 1981; 824-7

Somerfield MR, Weisman CS, Ury W, et al. Physician practices in the diagnosis of dementing disorders. *J Am Geriatr Soc.* 1991; 39: 172–5. [PubMed]

/Spector WD, Jackson ME. Correlates of disruptive behaviors in nursing homes: a reanalysis. *J Aging Health.* 1994; 6: 173–84. [PubMed]

Spitzer RL, Williams JBW, Kroenke K, et al. Utility of a new procedure for diagnosing mental disorders in primary care. The PRIME-MD 1000 Study.
JAMA. 1994; 272: 1749–56. [PubMed]

/Spreen O, Strauss E. A compendium of neuropsychological tests: administration, norms, and commentary , New York: Oxford University Press;1991. . –.

Sroka H, Elizan TS, Yahr MD, et al. Organic mental syndrome and confusional states in Parkinson's disease: relationship to computerized tomographic signs of cerebral atrophy. *Arch Neurol.* 1981; 38: 339–42. [PubMed]

Steele C, Rovner B, Chase GA, et al. Psychiatric symptoms and nursing home placement of patients with Alzheimer's disease. *Am J Psychiatry.* 1990; 147: 1049–51. [PubMed]

Stern Y, Albert M, Brandt J, et al. Utility of extrapyramidal signs and psychosis as predictors of cognitive and functional decline, nursing home admission, and death in Alzheimer's disease: prospective analysis from the Predictors Study.
Neurology. 1994; 44: 2300–7. [PubMed]

Stern Y, Gurland B, Tatemichi TK, et al. Influence of education and occupation on the incidence of Alzheimer's disease. *JAMA.* 1994; 271: 1004–10. [PubMed]

Storandt M, Botwinick J, Danziger WL, et al. Psychometric differentiation of mild senile dementia of the Alzheimer's type. *Arch Neurol.* 1984; 41: 497–9. [PubMed]

/Storandt M, Stone K, LaBarge E. Deficits in reading performance in very mild dementia of the Alzheimer type. *Neuropsychology.* 1995; ; 9: 174–5.

Stoudemire A, Hill C, Gulley LR, et al. Neuropsychological and biomedical assessment of depression-dementia syndromes. *J Neuropsychiatry Clin Neurosci.* 1989; 1: 347–61. [PubMed]

Strauss ME, Pasupathi M, Chatterjee A. Concordance between observers in descriptions of personality change in Alzheimer's disease. *Psychol Aging.* 1993; 8: 475–80. [PubMed]

Sultzer DL, Levin HS, Mahler ME, et al. A comparison of psychiatric symptoms in vascular dementia and Alzheimer's disease. *Am J Psychiatry.* 1993; 150: 1806–12. [PubMed]

Teri L, McCurry SW, Edland SD, et al. Cognitive decline in Alzheimer's disease: a longitudinal investigation of risk factors for accelerated decline.
J Gerontol. 1995; 50A: M49–55.

Teri L, Wagner A. Alzheimer's disease and depression.
J Consult Clin Psychol. 1992; 60: 379–91. [PubMed]

/Terry RD, Katzman R, Bick KL, editors. Alzheimer's disease , New York:Raven Press; 1994. –.

Tombaugh TN, McIntyre NJ. The Mini-Mental State Examination: a comprehensive review. *J Am Geriatr Soc.* 1992; 40: 922–35. [PubMed]

Torian L, Davidson E, Fulop G, et al. The effect of dementia on acute care in a geriatric medical unit. *Int Psychogeriatr.* 1992; 4: 231–9. [PubMed]

Uhlmann RF, Larson EB. Effect of education on the Mini-Mental State Examination as a screening test for dementia. *J Am Geriatr Soc.* 1991; 39: 876–80. [PubMed]

/U.S. Department of Veterans Affairs. Dementia: guidelines for diagnosis and treatment, 1989 (revised). VA Publication No. IB 18-3. pp. –.

van der Cammen TJM, van Harskamp F, Stronks DL, et al. Value of the Mini-Mental State Examination and informants' data for the detection of dementia in geriatric outpatients. *Psychol Rep.* 1992; 71: 1003–9. [PubMed]

van Duijn CM, Clayton D, Chandra V, et al. Familial aggregation of Alzheimer's disease and related disorders: a collaborative re-analysis of case-control studies *Int J Epidemiol* 1991. 20:(suppl 2):S13–S20. [PubMed].

/Victor M, Adams RD, Collins GH. The Wernicke-Korsakoff syndrome and related neurologic disorders due to alcoholism and malnutrition. 2nd ed. Contemporary neurology series , Philadelphia (PA):FA Davis;1989. . –.

Vitaliano PP, Breen AR, Albert MS, et al. Memory, attention, and functional status in community-residing Alzheimer type dementia patients and optimally healthy aged individuals. *J Gerontol.* 1984; 39: 58–64. [PubMed]

Vitaliano PP, Russo J, Breen AR, et al. Functional decline in the early stages of Alzheimer's disease. *J Psychol Aging.* 1986; 1: 41–6.

/Wechsler D. The Wechsler adult intelligence scale revised , New York: The Psychological Corporation;1981.

Weinberger M, Samsa GP, Schmader K, et al. Comparing proxy and patients' perceptions of patients' functional status: results from an outpatient geriatric clinic. *J Am Geriatr Soc.* 1992; 40: 585–8. [PubMed]

/Weis K. Personal communication: review of Medicare inpatient claims for 1992. 1992.

/Wells CE. Dementia. 2nd ed , Philadelphia (PA):FA Davis;1977. –.

Welsh K, Butters N, Hughes J, et al. Detection of abnormal memory decline in mild cases of Alzheimer's disease using CERAD neuropsychological measures. *Arch Neurol.* 1991; 48: 278–81. [PubMed]

Welsh KA, Butters N, Hughes JP, et al. Detection and staging of dementia in Alzheimer's disease: use of the neuropsychological measures developed for the Consortium to Establish a Registry for Alzheimer's Disease (CERAD). *Arch Neurol.* 1992; 49: 448–52. [PubMed]

Welsh KA, Butters N, Mohs RC, et al. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD), Part V: a normative study of the neuropsychological battery. *Neurology.* 1994; 44: 609–14. [PubMed]

White H, Davis PB. Cognitive screening tests: an aid in the care of elderly outpatients. *J Gen Intern Med.* 1990; 5: 438–45. [PubMed]

/Whitehouse PJ, editor. Dementia , Philadelphia (PA):FA Davis; 1993. –.

Wild KV, Kaye JA, Oken BS. Early noncognitive change in Alzheimer's disease and healthy aging. *J Geriatr Psychiatry Neurol.* 1994; 7: 199–205. [PubMed]

/Wilder DE, Cross P, Chen J, et al. Operating characteristics of brief screens for dementia in a multicultural population. *Am J Geriatr Psychiatry.* 1995; 3: 96–107.

/Wilder DE, Gurland BJ, Chen J, et al. Interpreting subject and informant reports of

function in screening for dementia. *Int J Geriatr Psychiatry.* 1994; 9: 887–96.

/Williamson J, Stokoe IH, Gray S, et al. Old people at home: their unreported needs. *Lancet.* 1964; i: 1117–20. [PubMed]

Wisniewski KE, Wisniewski HM, Wen GY. Occurrence of neuropathological changes and dementia of Alzheimer's disease in Down syndrome. *Ann Neurol.* 1985; 7: 278–82.

Wragg RE, Jeste DV. Overview of depression and psychosis in Alzheimer's disease. *Am J Psychiatry.* 1989; 146: 577–87. [PubMed]

/Wurtman RJ, Corkin S, Growdon JH, et al., editors. Advances in neurology, Vol. 51: Alzheimer's disease , New York:Raven Press; 1990. . –.

/Yahr MD, Bergmann KJ, editors. Advances in neurology, Vol. 45. Parkinson's disease , New York: Raven Press; 1986. –.

Yesavage JA. Geriatric Depression Scale. *Psychopharmacol Bull.* 1988; 24: 709–11. [PubMed]

/Yesavage JA. The use of self-rating depression scales in the elderly. In: Poon LW, editor. Handbook for clinical memory assessment of older adults , Washington (DC): American Psychological Association; 1986. p. 213–7.

Yesavage JA, Brink TL, Rose TL, et al. Development and validation of a geriatric screening scale: a preliminary report. *J Psychiatr Res.* 1983; 17: 37–49.

Yesavage JA, Brooks JO III, Taylor J, et al. Development of aphasia, apraxia, and agnosia and decline in Alzheimer's disease. *Am J Psychiatry.* 1993; 150: 742–7. [PubMed]

/Zec RF. Neuropsychological functioning in Alzheimer's disease. In: Parks RW, Zec RF, Wilson RS, editors. Neuropsychology of Alzheimer's disease and other dementias , New York: Oxford University Press; 1993. p. 3–80.

Zhang M, Katzman R, Salmon D, et al. The prevalence of dementia and Alzheimer's disease in Shanghai, China: impact of age, gender, and education. *Ann Neurol.* 1990; 27: 428–37. [PubMed]