



## NATIONAL GUIDELINE CLEARINGHOUSE™ (NGC) GUIDELINE SYNTHESIS

### ASSESSMENT AND DIAGNOSIS OF ALZHEIMER'S DISEASE AND RELATED DEMENTIAS

#### Guidelines

1. American Academy of Neurology (AAN). [Practice parameter: diagnosis of dementia \(an evidence-based review\): report of the Quality Standards Subcommittee of the American Academy of Neurology](#). Neurology 2001 May 8;56(9):1143-53. [147 references]
2. American Medical Directors Association (AMDA). [Dementia](#). Columbia (MD): American Medical Directors Association (AMDA); 2005. 28 p. [20 references]
3. Scottish Intercollegiate Guidelines Network (SIGN). [Management of patients with dementia. A national clinical guideline](#). Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2006 Feb. 53 p. (SIGN publication; no. 86). [183 references]

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#### INTRODUCTION:

A direct comparison of the American Academy of Neurology (AAN), American Medical Directors Association (AMDA) and Scottish Intercollegiate Guidelines Network (SIGN) recommendations for the assessment and diagnosis of Alzheimer's disease (AD) and related dementias is provided in the tables, below.

The guidelines differ considerably in scope. All of the guidelines address AD, as well as related dementias, such as dementia related to vascular disease (VAD), dementia with Lewy bodies (DLB), frontotemporal dementia (FTD), and Creutzfeldt-Jakob disease (CJD). The AAN and SIGN guidelines address the clinical and technical aspects of the diagnostic work-up in greatest detail, including neuroimaging and laboratory tests. The AMDA guideline, which is specific to the long-term care setting, focuses primarily on recognition and assessment of the patient with diagnosed or suspected AD (or other dementia) in order to meet his or her ongoing care needs. In addition to diagnosis, the AMDA and SIGN guidelines consider treatment, monitoring and management of patients with AD or other dementias. These topics are beyond the scope of this synthesis (see the NGC synthesis, [Alzheimer's Disease and Related Dementias. Part III. Treatment](#)).

[Table 1](#) compares the scope of each of the guidelines. [Table 2](#) compares recommendations for the assessment and diagnosis of AD and related dementias. [Table 3](#) compares the potential benefits and harms associated with the implementation of each guideline. Two of the guidelines, AAN and SIGN, rank the level of evidence supporting their major recommendations; the definitions of these rating schemes are provided in [Table 4](#). Following the content comparison tables, the areas of agreement and differences among the guidelines are identified.

### **Related Guidelines**

- California Workgroup on Guidelines for Alzheimer's Disease Management/Alzheimer's Association of Los Angeles (CWGAD/AALA). [Guidelines for Alzheimer's disease management](#). Los Angeles (CA): Alzheimer's Association of Los Angeles, Riverside and San Bernardino Counties; 2002 Jan 1. 52 p. [296 references]

### **Abbreviations:**

- AAN, American Academy of Neurology
- AD, Alzheimer's disease
- AMDA, American Medical Directors Association
- CJD, Creutzfeldt-Jakob disease
- CT, computed tomography
- DAT, dementia of the Alzheimer's type
- DLB, dementia with Lewy bodies
- DSM-IIIR, Diagnostic and Statistical Manual, 3<sup>rd</sup> edition, revised
- DSM-IV, Diagnostic and Statistical Manual, 4<sup>th</sup> edition
- FTD, frontotemporal dementia
- MMSE, Mini-Mental State Examination
- MRI, magnetic resonance imaging
- PET, positron emission tomography
- SIGN, Scottish Intercollegiate Guidelines Network
- SPECT, single photon emission computed tomography
- VAD, vascular dementia

**TABLE 1: COMPARISON OF SCOPE AND CONTENT**

<b>Objective And Scope</b>	
<b>AAN (2001)</b>	<ul style="list-style-type: none"> <li>• To update the 1994 practice parameter for the diagnosis of dementia in the elderly</li> <li>• To highlight and to update major areas of current interest and investigation in the diagnosis of dementia in the elderly</li> </ul>
<b>AMDA (2005)</b>	<ul style="list-style-type: none"> <li>• To offer care providers and practitioners in long-term care facilities a systematic approach to recognizing, assessing, treating, and monitoring patients with dementia, including impaired cognition and problematic behavior</li> <li>• To help practitioners to provide dementia patients with a systematic assessment and care plan, leading to appropriate management that maximizes functioning and quality of life and minimizes the likelihood of complications and functional decline</li> </ul>
<b>SIGN (2006)</b>	<ul style="list-style-type: none"> <li>• To present evidence-based recommendations for the management of dementia</li> <li>• To consider investigations and interventions in which direct benefit to the patient can be demonstrated</li> </ul>
<b>Target Population</b>	
<b>AAN (2001)</b>	Elderly patients (over age 65) undergoing an initial assessment for dementia
<b>AMDA (2005)</b>	Elderly individuals and/or residents of long-term care facilities who have, or are suspected of having, dementia
<b>SIGN (2006)</b>	Patients with all stages of dementia excluding mild cognitive impairment
<b>Intended Users</b>	
<b>AAN (2001)</b>	Physicians Psychologists/Non-physician Behavioral Health Clinicians
<b>AMDA (2005)</b>	Advanced Practice Nurses Allied Health Personnel Dietitians Nurses Pharmacists Physicians Social Workers

<b>SIGN (2006)</b>	Advanced Practice Nurses Nurses Occupational Therapists Physical Therapists Physician Assistants Physicians Psychologists/Non-physician Behavioral Health Clinicians
<b>Interventions And Practices Considered</b>	
<b>AAN (2001)</b>	<ol style="list-style-type: none"> <li>1. Diagnostic criteria <ol style="list-style-type: none"> <li>a. Dementia <ul style="list-style-type: none"> <li>• Diagnostic and Statistical Manual, 3<sup>rd</sup> edition, revised (DSM-IIIR)</li> </ul> </li> <li>b. Alzheimer's disease (AD) <ul style="list-style-type: none"> <li>• National Institute of Neurologic, Communicative Disorders and Stroke-Alzheimer's disease and related Disorders Association (NINCDS-ADRDA)</li> <li>• Diagnostic and Statistical Manual, 3<sup>rd</sup> edition, revised (DSM-IIIR)</li> </ul> </li> <li>c. Vascular dementia (VAD) <ul style="list-style-type: none"> <li>• Hachinski Ischemic Index</li> </ul> </li> <li>d. Dementia with Lewy bodies (DLB) <ul style="list-style-type: none"> <li>• Consensus guidelines, consortium on DLB</li> </ul> </li> <li>e. Frontotemporal dementia (FTD) <ul style="list-style-type: none"> <li>• Consensus guidelines</li> </ul> </li> <li>f. Creutzfeldt-Jakob disease (CJD)</li> </ol> </li> <li>2. Neuroimaging <ol style="list-style-type: none"> <li>a. Computed tomography (CT)</li> <li>b. Magnetic resonance imaging (MRI)</li> <li>c. Single photon emission computed tomography (SPECT)</li> <li>d. Positron emission tomography (PET)</li> </ol> </li> <li>3. Other assessments <ol style="list-style-type: none"> <li>a. Genetic testing (considered but not recommended)</li> <li>b. Cerebrospinal fluid (CSF) (considered but not recommended for routine use)</li> <li>c. Depression</li> <li>d. Vitamin B<sub>12</sub> status</li> <li>e. Thyroid function</li> <li>f. Common metabolic abnormalities</li> <li>g. Syphilis (considered but not recommended for routine use)</li> </ol> </li> </ol>
<b>AMDA (2005)</b>	<ol style="list-style-type: none"> <li>1. Medical history and physical examination</li> <li>2. Diagnostic criteria <ol style="list-style-type: none"> <li>a. Dementia <ul style="list-style-type: none"> <li>• Diagnostic and Statistical Manual, 4<sup>th</sup> edition (DSM-IV)</li> </ul> </li> </ol> </li> </ol>

	<ul style="list-style-type: none"> <li>b. Alzheimer's Disease (AD) <ul style="list-style-type: none"> <li>• Diagnostic and Statistical Manual, 4<sup>th</sup> edition (DSM-IV)</li> </ul> </li> <li>3. Functional status assessment <ul style="list-style-type: none"> <li>a. Activities of Daily Living portion of Minimum Data Set (MDS)</li> <li>b. Barthel Index</li> <li>c. Functional Activities Questionnaire</li> </ul> </li> <li>4. Cognitive status assessment <ul style="list-style-type: none"> <li>a. MMSE</li> <li>b. Clock Drawing test</li> <li>c. Blessed Orientation-memory Concentration Test</li> </ul> </li> <li>5. Neuroimaging <ul style="list-style-type: none"> <li>a. Computed tomography (CT)</li> <li>b. Magnetic resonance imaging (MRI)</li> </ul> </li> <li>6. Other assessments <ul style="list-style-type: none"> <li>a. Neuropsychological testing</li> <li>b. Medical assessment/diagnostic work-up as needed</li> <li>c. Depression</li> <li>d. Behavior</li> <li>e. Psychosocial wellbeing</li> </ul> </li> </ul> <p><b>Note:</b> This guideline also addresses treatment and monitoring of patients with AD and dementia. See the NGC guideline synthesis, <a href="#">Alzheimer's Disease and Related Dementias, Part III. Treatment.</a></p>
<p><b>SIGN (2006)</b></p>	<ul style="list-style-type: none"> <li>1. Diagnostic Criteria <ul style="list-style-type: none"> <li>a. Alzheimer's disease (AD) <ul style="list-style-type: none"> <li>• Diagnostic and Statistical Manual, 4<sup>th</sup> edition (DSM-IV)</li> <li>• National Institute of Neurologic, Communicative Disorders and Stroke-Alzheimer's disease and related Disorders Association (NINCDS-ADRDA)</li> </ul> </li> <li>b. Vascular dementia (VAD) <ul style="list-style-type: none"> <li>• Hachinski Ischaemic Score</li> <li>• National Institute of Neurological Disorders and Stroke-Association Internationale pour la Recherche et l'Enseignement en Neurosciences (NINDS-AIREN)</li> </ul> </li> <li>c. Dementia with Lewy bodies (DLB) <ul style="list-style-type: none"> <li>• Consensus guidelines, consortium on DLB</li> </ul> </li> <li>d. Frontotemporal dementia (FTD) <ul style="list-style-type: none"> <li>• Lund-Manchester criteria</li> </ul> </li> </ul> </li> <li>2. Medical history</li> <li>3. Cognitive assessment <ul style="list-style-type: none"> <li>a. MMSE</li> <li>b. Addenbrooke's Cognitive Examination (ACE)</li> <li>c. Informant Questionnaire on Cognitive Decline in the Elderly</li> </ul> </li> </ul>

	<p>(IQCODE)</p> <p>4. Neuroimaging</p> <ol style="list-style-type: none"> <li>a. Computed tomography (CT)</li> <li>b. Magnetic resonance imaging (MRI)</li> <li>c. Positron emission tomography (PET)</li> <li>d. Single-photon emission computed tomography (SPECT)</li> </ol> <p>5. Other assessments</p> <ol style="list-style-type: none"> <li>a. Cerebrospinal fluid (CSF) and electroencephalography (EEG) (considered but not recommended for routine use)</li> <li>b. Comorbid conditions, including depression</li> <li>c. Neuropsychological testing</li> </ol> <p><b>Note:</b> This guideline also addresses treatment and monitoring of patients with AD and dementia. See the NGC guideline synthesis, <a href="#">Alzheimer's Disease and Related Dementias. Part III. Treatment.</a></p>
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<b>TABLE 2: COMPARISON OF RECOMMENDATIONS FOR ASSESSMENT AND DIAGNOSIS OF ALZHEIMER'S DISEASE AND RELATED DEMENTIAS</b>	
<b>Definitions and Diagnostic Criteria</b>	
<b>AAN (2001)</b>	<ul style="list-style-type: none"> <li>• The <i>Diagnostic and Statistical Manual</i>, 3rd edition, revised (DSM-IIIR) definition of dementia, which is identical to the DSM-IV definition, is reliable and should be used routinely (<b>Guideline</b>).</li> </ul> <p>The DSM-IIIR states:</p> <p>"The essential feature of Dementia is impairment in short-and long-term memory, associated with impairment in abstract thinking, impaired judgment, other disturbances of higher cortical function, or personality change. The disturbance is severe enough to interfere significantly with work or usual social activities or relationships with others. The diagnosis of Dementia is not made if these symptoms occur...in Delirium..."</p> <ul style="list-style-type: none"> <li>• The National Institute of Neurologic, Communicative Disorders and Stroke—Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) for the diagnosis of probable AD or the <i>Diagnostic and Statistical Manual</i>, 3rd edition, revised (DSM-III-R) criteria for dementia of the Alzheimer type (DAT) should be routinely used (<b>Guideline</b>).</li> <li>• The Hachinski Ischemic Index criteria may be of use in the diagnosis of cerebrovascular disease in dementia (<b>Option</b>).</li> <li>• The Consortium for DLB diagnostic criteria may be of use in clinical practice (<b>Option</b>).</li> </ul>

	<ul style="list-style-type: none"> <li>• The Consensus diagnostic criteria for FTD may be of use in clinical practice <b>(Option)</b>.</li> <li>• Clinical criteria for CJD should be used in rapidly progressive dementia syndromes <b>(Guideline)</b>.</li> </ul>
<p><b>AMDA (2005)</b></p>	<p><b>Definition</b></p> <p>Dementia is a syndrome (a collection of signs and symptoms) characterized by progressive decline in multiple areas of cognitive function, which eventually produces significant deficits in self-care and social and occupational performance.</p> <p><b>Diagnostic Criteria for Dementia</b></p> <p>A. The development of multiple cognitive deficits manifested by both:</p> <ol style="list-style-type: none"> <li>1. Memory impairment (impaired ability to learn new information or to recall previously learned information)</li> <li>2. One or more of the following cognitive disturbances: <ul style="list-style-type: none"> <li>• Aphasia (language disturbance)</li> <li>• Apraxia (impaired ability to carry out motor activities despite intact motor function)</li> <li>• Agnosia (failure to recognize or identify objects despite intact sensory function)</li> <li>• Disturbance in executive functioning (i.e., planning, organizing, sequencing, abstracting)</li> </ul> </li> </ol> <p>B. The cognitive deficits in criteria A(1) and A(2) each cause significant impairment in social or occupational functioning and represent a significant decline from a previous level of functioning</p> <p><b>Note:</b> Adapted from DSM-IV.</p> <p><b>Diagnostic Criteria for Alzheimer's Disease</b></p> <p>A. The development of multiple cognitive deficits manifested by both:</p> <ol style="list-style-type: none"> <li>1. Memory impairment (impaired ability to learn new information or to recall previously learned information) and</li> <li>2. One or more of the following cognitive disturbances: <ul style="list-style-type: none"> <li>• Aphasia (language disturbance)</li> <li>• Apraxia (impaired ability to carry out motor activities despite intact motor function)</li> <li>• Agnosia (failure to recognize or identify objects despite intact sensory function)</li> <li>• Disturbance in executive functioning (i.e., planning, organizing, sequencing, abstracting)</li> </ul> </li> </ol> <p>B. The cognitive deficit in criteria A(1) and A(2) causes significant impairment in social or occupational functioning and represents a significant decline from a previous level of functioning.</p> <p>C. The course is characterized by gradual onset and continuing cognitive decline. The cognitive deficits in A(1) and A(2) are not</p>

	<p>due to any of the following:</p> <ol style="list-style-type: none"> <li>1. Other central nervous system conditions that cause progressive deficits in memory and cognition (e.g., cerebrovascular disease, Parkinson's disease, Huntington's disease, subdural hematoma, normal pressure hydrocephalus, brain tumor)</li> <li>2. Systemic conditions that are known to cause dementia (e.g., hypothyroidism, vitamin B<sub>12</sub>, or folic acid deficiency, niacin deficiency, hypercalcemia, neurosyphilis, HIV infection)</li> <li>3. Substance-induced conditions <ul style="list-style-type: none"> <li>• The deficits do not occur exclusively during the course of delirium.</li> <li>• The disturbance is not better accounted for by another axis I disorder (e.g., major depressive disorder, schizophrenia).</li> </ul> </li> </ol> <p><b>Note:</b> Adapted from DSM-IV.</p>
<p><b>SIGN (2006)</b></p>	<p><b>Definitions</b></p> <p><u>Dementia</u></p> <p>A generic term indicating a loss of intellectual functions including memory, significant deterioration in the ability to carry out day-to-day activities, and often, changes in social behaviour.</p> <p><u>Alzheimer's Disease</u></p> <p>The most common cause of dementia is Alzheimer's disease (AD). Symptoms include memory problems, a progressive deterioration in the ability to perform basic activities of daily living (ADL), and behaviour changes, mainly apathy and social withdrawal, but also behavioural disturbances. Alzheimer's disease causes abnormal function and eventual death of selected nerve cells in the brain. The average survival period for patients following diagnosis is 8 to 10 years.</p> <p><u>Vascular Dementia</u></p> <p>The role of vascular disease in the aetiology of dementia is complex and controversial. In some cases there appears to be a direct chronological relationship between significant cerebrovascular events and the onset of dementia. Consequently patients may present with signs of stroke or other vascular problems, for example, ischaemic heart disease or hypertension. Onset may be abrupt or there may be periods of sudden decline followed by relative stability. Physical problems such as urinary incontinence, decreased mobility and balance problems are more commonly seen in people with vascular dementia</p>



(VaD) than in people with Alzheimer's disease.

### Dementia with Lewy Bodies

Characteristic features of dementia with Lewy bodies (DLB) are fluctuation of awareness from day-to-day and signs of parkinsonism such as tremor, rigidity and slowness of movement or poverty of expression. Visual hallucinations or delusions occur frequently. Falls are also common. DLB has a similar pathological basis to Parkinson's disease dementia and both are associated with progressive cognitive decline and parkinsonism. Approximately three quarters of older people with Parkinson's disease develop dementia after 10 years.

### Fronto-temporal Dementia

Fronto-temporal dementia (FTD) is uncommon by comparison to Alzheimer's disease or vascular dementia but represents a significant proportion of people who present with dementia under the age of 65. Changes in behaviour such as disinhibition, lack of judgement, loss of social awareness and loss of insight are much more common than memory problems. Disturbance of mood, speech and continence are frequent. A positive family history of a similar disorder is not uncommon.

### Mixed Dementias

Mixtures of two or more of the active dementias can be found in the same person, with one or other usually dominating. Studies suggest that the interaction between vascular disease and the core features of Alzheimer's disease is extremely complex and that rigid boundaries between subtypes of dementia may be unduly artificial. Response to treatment or side effects from treatment in people with mixed dementia may be different from those in people with a specific diagnosis.

### Creutzfeldt-Jakob Disease

Creutzfeldt-Jakob disease (CJD) is a very uncommon illness in which an abnormal protein accumulates in the brain and leads to rapid destruction of nerve cells. Tremor, impaired mobility and balance problems are common as are behavioural and mood disturbance. Death within one to two years of the onset of clinical symptoms is common.

### **Diagnostic Criteria**

**B** - DSM-IV or National Institute of Neurologic, Communicative Disorders and Stroke-Alzheimer's disease and related Disorders Association (NINCDS-ADRDA) criteria should be used for the diagnosis of AD.

**B** - The Hachinski Ischaemic Scale or National Institute of Neurological

	<p>Disorders and Stroke--Association Internationale pour la Recherche et l'Enseignement en Neurosciences (NINDS-AIRENS) criteria may be used to assist in the diagnosis of vascular dementia.</p> <p><b>C</b> - Diagnostic criteria for DLB and FTD should be considered in clinical assessment.</p>
<p><b>Initial Assessment</b></p>	
<p><b>AAN (2001)</b></p>	<p><b>Diagnostic Criteria</b></p> <ul style="list-style-type: none"> <li>• The <i>Diagnostic and Statistical Manual</i>, 3rd edition, revised (DSM-IIIR) definition of dementia, which is identical to the DSM-IV definition, is reliable and should be used routinely <b>(Guideline)</b>.</li> <li>• The National Institute of Neurologic, Communicative Disorders and Stroke—Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) for the diagnosis of probable AD or the <i>Diagnostic and Statistical Manual</i>, 3<sup>rd</sup> edition, revised (DSM-III-R) criteria for dementia of the Alzheimer type (DAT) should be routinely used <b>(Guideline)</b>.</li> <li>• The Hachinski Ischemic Index criteria may be of use in the diagnosis of cerebrovascular disease in dementia <b>(Option)</b>.</li> <li>• The Consortium for DLB diagnostic criteria may be of use in clinical practice <b>(Option)</b>.</li> <li>• The Consensus diagnostic criteria for FTD may be of use in clinical practice <b>(Option)</b>.</li> <li>• Clinical criteria for CJD should be used in rapidly progressive dementia syndromes <b>(Guideline)</b>.</li> </ul> <p><b>Screening for Comorbidities</b></p> <ul style="list-style-type: none"> <li>• Depression is a common, treatable comorbidity in patients with dementia and should be screened for <b>(Guideline)</b>.</li> <li>• [Vitamin] B<sub>12</sub> deficiency is common in the elderly, and B<sub>12</sub> levels should be included in routine assessments of the elderly. <b>(Guideline)</b>.</li> <li>• Because of its frequency, hypothyroidism should be screened for in elderly patients. <b>(Guideline)</b>.</li> <li>• Unless the patient has some specific risk factor or evidence of prior syphilitic infection, or resides in one of the few areas in the United States with high numbers of syphilis cases, screening for the disorder in patients with dementia is not justified <b>(Guideline)</b>.</li> </ul>
<p><b>AMDA (2005)</b></p>	<p><b>Recognition</b></p> <p>Step 1. Does the patient have a history of dementia?</p> <p>Review available information about the patient's recent or past</p>

physical, functional, cognitive, and behavioral status.

Step 2. Does the patient have current signs or symptoms of dementia?

Nurses, nursing assistants, social workers, therapists, and practitioners should observe the patient's current physical, functional, and psychosocial status. Function may be assessed with one of several instruments (e.g., Activities of Daily Living [ADL], portion of the Minimum Data Set [MDS], Barthel Index, Functional Activities Questionnaire [FAQ]).

Cognition may be assessed using the MMSE, Clock Drawing test, Blessed Orientation-Memory-Concentration Test, or other comparable instruments. To help ensure reliability, each facility should choose a standard battery of tests for routine use, reserving others for special situations.

### **Assessment**

Step 3. Determine if further work-up is useful and appropriate.

The primary aim of a diagnostic work-up in patients with dementia is identification of potentially treatable conditions.

Step 4. Verify that the patient meets the criteria for a diagnosis of dementia.

Patients most likely to have dementia manifest impaired mental status and function. If the patient meets the criteria for a diagnosis of dementia, proceed through the subsequent steps in this guideline. If the diagnosis of dementia is not made or confirmed, or if a patient with a prior diagnosis of dementia has a recent significant condition change, consider other causes for the patient's symptoms before concluding either that the patient has dementia or that recent changes are due to dementia.

NGC Note: Refer to Table 8, *Diagnostic Criteria for Dementia*, and Table 9, *Diagnostic Criteria for Alzheimer's Disease* in original guideline document.

Step 5. Identify the cause(s) of dementia.

Determining the cause may help to prevent further deterioration or may establish a prognosis.

Step 6. Identify the patient's strengths and deficits.

Soon after admission or a significant condition change, assess the patient's capabilities in various domains (refer to Table 10 in the original guideline document), using an appropriate assessment

	<p>instrument (see Step 2, above).</p> <p>Step 7. Define the significance of the patient's symptoms, impairments, and deficits.</p> <p>These should be an important consideration in care planning.</p> <p>Step 8. Identify triggers for disruptive behavior.</p> <p>Identifying these triggers enables the use of targeted interventions to prevent or manage the disruptive behavior.</p> <p>For additional details of each step, see the original guideline document. This guideline includes an algorithm, <a href="#">Dementia</a>, that is to be used in conjunction with the clinical practice guideline.</p>
<p><b>SIGN (2006)</b></p>	<p><b>Initial Cognitive Testing</b></p> <p><b>B</b> - In individuals with suspected cognitive impairment, the MMSE should be used in the diagnosis of dementia.</p> <p><b>Good Practice Point.</b> Initial cognitive testing can be improved by the use of Addenbrooke's Cognitive Examination.</p> <p><b>Good Practice Point.</b> A questionnaire, such as the IQCODE, completed by a relative or friend may be used in the diagnosis of dementia.</p> <p><b>Screening for Comorbid Conditions</b></p> <p><b>B</b> - As part of the assessment for suspected dementia, the presence of comorbid depression should be considered.</p> <p><b>Good Practice Point.</b> Physical investigations including laboratory tests should be selected on clinical grounds according to history and clinical circumstances.</p>
<p><b>Neuroimaging And Other Laboratory Tests</b></p>	
<p><b>AAN (2001)</b></p>	<ul style="list-style-type: none"> <li>• Structural neuroimaging with either a noncontrast computed tomography or magnetic resonance scan in the initial evaluation of patients with dementia is appropriate. <b>(Guideline).</b></li> <li>• Linear or volumetric magnetic resonance or computed tomography measurement strategies for the diagnosis of AD are not recommended for routine use at this time <b>(Guideline).</b></li> <li>• For patients with suspected dementia, single photon emission computed tomography (SPECT) cannot be recommended for routine use in either initial or differential diagnosis as it has not demonstrated superiority to clinical criteria <b>(Guideline).</b></li> </ul>

	<ul style="list-style-type: none"> <li>• Positron emission tomography (PET) imaging is not recommended for routine use in the diagnostic evaluation of dementia at this time <b>(Guideline)</b>.</li> <li>• Genetic testing of patients with suspected DLB and CJD is not recommended <b>(Guideline)</b>.</li> <li>• Routine use of apolipoprotein E (APOE) genotyping in patients with suspected AD is not recommended at this time <b>(Guideline)</b>.</li> <li>• There are no other genetic markers recommended for routine use in the diagnosis of AD <b>(Guideline)</b>.</li> <li>• Testing for tau mutations or AD gene mutations is not recommended for routine evaluation in patients with FTD at this time <b>(Guideline)</b>.</li> <li>• There are no cerebrospinal fluid or other biomarkers recommended for routine use in determining the diagnosis of AD at this time <b>(Guideline)</b>.</li> <li>• The cerebrospinal fluid 14-3-3 protein is recommended for confirming or rejecting the diagnosis of Creutzfeldt—Jakob disease in clinically appropriate circumstances <b>(Guideline)</b>.</li> </ul>
<b>AMDA (2005)</b>	<p><b>Step 5.</b> Identify the cause(s) of dementia</p> <p>A neurological, psychological, or psychiatric assessment may help to guide additional evaluation. Some tests (e.g., computed tomography [CT] or magnetic resonance imaging [MRI] brain scans) may reveal the presence of a tumor, bleed or other structural abnormalities. However, structural abnormalities may not correspond to functional or cognitive impairments. Conversely, functional and cognitive impairments may exist despite unremarkable test results.</p> <p>Consider consultation with a specialist in neuropsychological testing or psychiatric disorders if basic evaluation and testing do not enable adequate assessment of the patient's conditions, identification of the causes of the patient's symptoms, or proper management. Formal neuropsychological testing may also be helpful when screening tests suggest compromise or when other factors, such as the patient's formal educational background, intelligence level, ethnic background, or command of English, complicate the screening process.</p>
<b>SIGN (2006)</b>	<p><b>The Use of Imaging</b></p> <p><b>C</b> - Structural imaging should ideally form part of the diagnostic workup of patients with suspected dementia.</p> <p><b>C</b> - Single photon emission controlled tomography (SPECT) may be used in combination with computed tomography (CT) to aid the differential diagnosis of dementia when the diagnosis is in doubt.</p> <p><b>The Role of Cerebrospinal Fluid and Electroencephalography</b></p>

	<p><b>B</b> - Cerebrospinal fluid (CSF) and Electroencephalography (EEG) examinations are not recommended as routine investigations for dementia.</p> <p><b>Good Practice Point.</b> CSF and EEG examinations may be useful where CJD is suspected.</p> <p><b>Neuropsychological Testing</b></p> <p><b>B</b> - Neuropsychological testing should be used in the diagnosis of dementia, especially in patients where dementia is not clinically obvious.</p> <p><b>Good Practice Point.</b> It may be useful to repeat neuropsychological testing after six to 12 months in patients where:</p> <ul style="list-style-type: none"> <li>• the diagnosis is unclear</li> <li>• measurement of the progression of deficits in a typical pattern supports a diagnosis of dementia and helps in differential diagnosis.</li> </ul>
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<b>TABLE 3: BENEFITS AND HARMS</b>	
<b>Benefits</b>	
<b>AAN (2001)</b>	<ul style="list-style-type: none"> <li>• Appropriate use of diagnostic criteria and laboratory tests for dementia</li> <li>• Appropriate recognition and treatment of depression, B<sub>12</sub> deficiency, and hypothyroidism, which are common comorbid conditions in elderly patients with dementia</li> </ul>
<b>AMDA (2005)</b>	<p><b>Expected Outcomes from Implementation of this Clinical Practice Guideline</b></p> <p>Implementation of this guideline should:</p> <ul style="list-style-type: none"> <li>• Identify patients who are at risk for new or progressive dementia</li> <li>• Identify the nature and causes of dementia in different patients</li> <li>• Make appropriate environmental modifications to maximize patient dignity, comfort and safety</li> <li>• Identify and manage potential sources of excess disability</li> <li>• Minimize preventable complications and functional decline</li> <li>• Manage dementia symptoms, consequences, and complications effectively and appropriately</li> </ul>

	<ul style="list-style-type: none"> <li>Respond appropriately to the changing needs of patients with dementia</li> </ul> <p><i>Anticipated care outcomes:</i> As a result of the above, the following patient-related outcomes may be anticipated:</p> <ul style="list-style-type: none"> <li>Maintained or improved function and quality of life prior to the end of life</li> <li>Reduced complications and negative consequences of the condition or its management</li> <li>Improved resource utilization</li> </ul>
<b>SIGN (2006)</b>	<p>Implementation of this guideline should:</p> <ul style="list-style-type: none"> <li>Improve early identification of dementia</li> <li>Allow early involvement of professional services in treatment</li> <li>Ensure that people receive clinically effective treatment at a point where both they and their carers will be able to appreciate the benefits</li> <li>Ensure that patients and carers have a better understanding of the illness and are able to adjust to difficulties as they arise</li> <li>Aid management of problems and difficulties, which can delay the need to go into a care home</li> </ul>
<b>Harms</b>	
<b>AAN (2001)</b>	Not stated
<b>AMDA (2005)</b>	Not stated
<b>SIGN (2006)</b>	Not stated

**TABLE 4: EVIDENCE RATING SCHEMES AND REFERENCES**

<b>AAN (2001)</b>	<p><b>Classification of Evidence</b></p> <p>I. Evidence provided by a well-designed prospective study in broad spectrum of persons with the suspected condition, using a "gold standard" for case definition, in which test is applied in a blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy.</p>
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	<p>II. Evidence provided by a well-designed prospective study of a narrow spectrum of persons with the suspected condition, or a well designed retrospective study of a broad spectrum of persons with an established condition (by "gold standard") compared with a broad spectrum of controls, in which test is applied in blinded evaluation, and enabling the assessment of appropriate tests of diagnostic accuracy.</p> <p>III. Evidence provided by a retrospective study in which either persons with the established condition or controls are of a narrow spectrum, and in which test is applied in a blinded evaluation.</p> <p>IV. Any design in which test is not applied in blinded evaluation OR evidence provided by expert opinion alone or in descriptive case series (without controls).</p> <p><b>Practice Recommendations Based on Classification of Evidence</b></p> <p><i>Standard.</i> Principle for patient management that reflects a high degree of clinical certainty (usually this requires Class I evidence that directly addresses the clinical question, or overwhelming Class II evidence when circumstances preclude randomized clinical trials).</p> <p><i>Guideline.</i> Recommendation for patient management that reflects moderate clinical certainty (usually this requires Class II evidence or a strong consensus of Class III evidence).</p> <p><i>Practice Option.</i> Strategy for patient management for which the clinical utility is uncertain (inconclusive or conflicting evidence or opinion).</p> <p><i>Practice Advisory.</i> Practice recommendation for emerging and/or newly approved therapies or technologies based on evidence from at least one Class I study. The evidence may demonstrate only a modest statistical effect or limited (partial) clinical response, or significant cost—benefit questions may exist. Substantial (or potential) disagreement among practitioners or between payers and practitioners may exist.</p>
<p><b>AMDA (2005)</b></p>	<p>The type of evidence supporting the recommendations is not specifically stated.</p> <p>The guideline was developed by interdisciplinary work groups using a process that combines evidence and consensus-based approaches.</p>
<p><b>SIGN (2006)</b></p>	<p><b>Levels of Evidence</b></p> <p><b>1++:</b> High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias</p> <p><b>1+:</b> Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias</p> <p><b>1-:</b> Meta-analyses, systematic reviews of RCTs, or RCTs with a high</p>



risk of bias

**2++:** High quality systematic reviews of case control or cohort studies  
High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal

**2+:** Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal

**2-:** Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal

**3:** Non-analytic studies (e.g., case reports, case series)

**4:** Expert opinion

### **Grades of Recommendations**

**Note:** The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

**Grade A:** At least one meta-analysis, systematic review of randomized controlled trials (RCTs), or RCT rated as 1++ and directly applicable to the target population; *or*

A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

**Grade B:** A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; *or*

Extrapolated evidence from studies rated as 1++ or 1+

**Grade C:** A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; *or*

Extrapolated evidence from studies rated as 2++

**Grade D:** Evidence level 3 or 4; *or*

Extrapolated evidence from studies rated as 2+

**Good Practice Points:** Recommended best practice based on the

clinical experience of the guideline development group.
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## **GUIDELINE CONTENT COMPARISON**

The American Academy of Neurology (AAN), American Medical Directors Association (AMDA) and Scottish Intercollegiate Guidelines Network (SIGN) present recommendations for the assessment and diagnosis of Alzheimer's disease (AD) and related dementias.

AAN and SIGN provide explicit reasoning behind their judgments and rank the level of evidence for each major recommendation; AMDA offers literature citations to support their major recommendations.

All three guidelines address AD, as well as related dementias, such as dementia related to vascular disease (VAD), dementia with Lewy bodies (DLB), frontotemporal dementia (FTD), and Creutzfeldt-Jakob disease (CJD). The guidelines differ in terms of their intended use, however. The AAN and SIGN guidelines address the components of the diagnostic work-up, including neuroimaging and other laboratory tests. In contrast, the AMDA guideline, which is specific to the long-term care setting, focuses on assessing the functional and cognitive status of the patient with diagnosed or suspected AD (or other dementia) in order to meet his or her management and care needs. In addition to assessment and diagnosis, the AMDA and SIGN guidelines consider treatment, monitoring and management of patients with AD or other dementias. These topics are addressed in a separate synthesis (see the NGC synthesis, [Alzheimer's Disease and Related Dementias. Part III. Treatment](#)).

### **Areas of Agreement**

#### *Diagnostic Criteria*

The AAN and AMDA guidelines agree that the definition of dementia found in the Diagnostic and Statistical Manual, 4<sup>th</sup> edition (DSM-IV), also found in the Diagnostic and Statistical Manual, 3rd edition, revised (DSM-III-R) should be used. For the diagnosis of AD specifically, AAN and SIGN agree that either the DSM-IV (or DSM-III-R) criteria or the National Institute of Neurological Disorders and Stroke-Alzheimer's disease and related Disorders Association (NINCDS-ADRDA) criteria should be used.

For the diagnosis of dementia related to cerebrovascular disease, AAN and SIGN both recommend use of the Hachinski Ischemic Index; SIGN also recommends the National Institute of Neurological Disorders and Stroke—Association Internationale pour la Recherche et l'Enseignement en Neurosciences (NINDS-AIRENS) criteria for this purpose.

#### *Initial Assessment*

The AMDA and SIGN guidelines recommend a detailed patient history and assessment of functional and cognitive status as the first steps to establish a diagnosis of dementia before proceeding with further investigations to assess the cause and nature of the dementia. There is general agreement on the cognitive and functional tests that are appropriate, such as the Mini-Mental State Examination (MMSE). All of the guidelines note that patients should also be screened for secondary causes of dementia and the presence of comorbid conditions such as depression. The AMDA and SIGN guidelines recommend obtaining information from reliable informants, family members or caregivers.

### *Neuroimaging and Other Laboratory Tests*

The AAN, AMDA, and SIGN guidelines agree that structural imaging — either computed tomography (CT) or magnetic resonance imaging (MRI) — are appropriate in the initial diagnosis of dementia. According to AAN, the existing data support the use of a neuroimaging examination — either a noncontrast CT or MR scan — under most circumstances at the time of the initial dementia assessment to identify pathology. Differences between these guidelines concerning neuroimaging are discussed below. AAN and SIGN agree that testing of cerebral spinal fluid (CSF) is not necessary for diagnosis of dementia or AD.

### **Areas of Differences**

The AAN and SIGN guidelines offer different recommendations regarding the use of quantitative neuroimaging in the diagnosis of AD. AAN recommends against linear and volumetric MRI, noting that no studies have determined the added value of measurements of hippocampal or entorhinal volume once a clinical diagnosis of AD has been made. The guideline states that measurement of hippocampal atrophy by MRI has low precision and may not be useful in clinical practice. In contrast, SIGN states that MRI indices such as hippocampal volumetry can support clinical diagnosis of early AD, assist in differential diagnosis of vascular dementia, and diagnose sporadic and variant CJD.

AAN and SIGN also differ concerning the value of functional neuroimaging, such as positron emission tomography (PET) and single photon emission computed tomography (SPECT). AAN recommends against routine use of SPECT in the initial or differential diagnosis of dementia. In contrast, SIGN states that SPECT in combination with CT may aid the differential diagnosis of dementia. According to SIGN, the value of SPECT in differentiating AD from VAD, DLB and FTD has been demonstrated. These differing recommendations may be due in part to the body of literature available during guideline development. The AAN guideline was published in 2001 and SIGN in 2006 and six of the ten studies cited by SIGN in its discussion of SPECT were published in 2000 or later.

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