

Clinical Diagnosis of Dementia

In this module, learn about clinical diagnosis of dementia and:

- The important components of the history and exam
- Methods of evaluating cognitive function
- The relevant diagnostic studies
- The differential diagnosis of dementia

When the clinical triggers described in [Dementia in Primary Care](#) raise suspicion of possible dementia, evaluation of the patient should include a history and physical exam that focus on specific areas of concern. Various diagnostic studies can be used as well to confirm the problem and assess the differential diagnosis. The physician also needs to know when referral is appropriate, and to understand that the slow progression of dementia may mean that a definitive diagnosis can only be made over an extended period of time.

HISTORY

The history should be obtained from the patient as well as an additional reliable informant. When diagnosing dementia, the important components of the history include:

- History of cognitive impairment signs and symptoms, including timing of earliest effects and rate of progression
- Current and past medical problems, including systemic diseases, neurological disorders, head trauma, alcohol or substance abuse, infectious or metabolic illnesses
- Functional status, focused on ADLs and IADLs – see *Table A* for the ADL and IADL forms, and *Table B* for the Functional Activities Questionnaire
- Current medications, with special attention to both prescription and non-prescription medications that have anti-cholinergic properties
- Family history, especially any early-onset dementia, neurological conditions, and vascular diseases
- Social history, including:
 - Family and social supports
 - Educational background
 - Literacy
 - Preferred language
 - Alcohol, tobacco, and other substance use

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PHYSICAL EXAM

The key elements of the physical exam include:

- General appearance and behavior, including hygiene, affect, and alertness
- Pulse and blood pressure, including any orthostatic changes
- Cardiac and pulmonary auscultation
- Neurologic exam
 - Focal deficits, including cranial nerves, motor and sensory exam of the extremities, coordination, balance and gait
 - Signs of Parkinson's disease, including cogwheeling, masked facies, bradykinesia, rigidity, and resting tremor

DIAGNOSTIC TESTING

The routine laboratory workup for dementia generally includes: CBC with differential, chemistry profile (with electrolytes, creatinine, calcium, glucose, and liver function tests), TSH, and vitamin B₁₂ levels. Other laboratory tests may be indicated in selected patients, including urinalysis, serologic tests for syphilis and/or HIV, tests for autoimmune diseases and vasculitis, and toxicology screens. Chest x-rays, EEGs, and exams of CSF (cerebrospinal fluid) are occasionally helpful.

Brain imaging (CT or MRI) is generally recommended in the evaluation of early or middle stage dementia. The American Academy of Neurology has stated that, "structural neuroimaging with either a noncontrast CT or MR scan in the routine initial evaluation of patients with dementia is appropriate." (Level of Evidence is "Guideline" only.) When dementia is diagnosed in the late stage and is typical for Alzheimer's, it may not be necessary to perform imaging studies.

Studies have been mixed about the value of brain imaging in dementia patients, and clinicians should bear in mind not only that abnormalities found may be unrelated to the patient's status but also that interventions may not lead to any improvement in symptoms. Evaluation of possible interventions related to abnormal imaging studies should involve experienced experts with a healthy dose of skepticism about the value of such interventions.

COGNITIVE TESTING

There is no single tool perfect for use in diagnosing dementia. All of the instruments that have been proposed have limitations. One of the biggest issues is that a tool with sufficient sensitivity to diagnose early dementia will also have a relatively low specificity—that is, a high false negative rate. A second major issue is the brevity of

the tool – an instrument short enough to use in clinical practice by necessity gives up a certain level of both sensitivity and specificity.

The Mini-Mental Status Exam (MMSE) (*Table A*) is the tool most widely used by healthcare professionals in the U.S., and it is the most comprehensive of the short tools available for evaluation as it tests multiple domains of cognitive function. The Blessed Information Memory Concentration (BIMC), Blessed Orientation Memory Concentration (BOMC), and the Short Test of Mental Status (STMS) are roughly equivalent to the MMSE though less widely used. It is important to note that all of these tests require adjustment for educational status, ethnicity, and socioeconomic status, and that there is no absolute cutoff for distinguishing normal from abnormal scores in individual patients.

The diagnosis of dementia requires identification of both memory loss and decline in an additional domain of cognitive function. The MMSE and the other short tests are excellent for identifying more advanced disease, but may fall short in assessing earlier symptoms. By necessity, each domain is tested only briefly. Tests of recent memory are the most discriminating measures overall in identifying dementia, but reliance on this criterion alone may miss those people for whom loss in another cognitive domain is the most prominent symptom. Declines in domains such as language ability, psychomotor performance, or executive function may also be early symptoms of dementia.

A comprehensive review of instruments was performed by the Agency for Health Care Policy and Research (now the Agency for Research in Health Care Quality) (Pfeffer et al, 1982), demonstrating that the presence of cognitive and functional decline can be documented in many different ways. Key points from that review include:

- The Functional Activity Questionnaire is the single best test for dementia, but it requires the presence of a reliable informant, usually a family member.
- The MMSE, BIMC, BOMC, and STMS are roughly equivalent.

Experts in the Michigan Primary Care Dementia Network have found a variety of individualized tests to be helpful in early assessment of dementia. None of these approaches have been rigorously tested in clinical trials:

- Testing “category fluency” – asking the patient to name as many items as possible in one minute, in a category like fruits and vegetables or animals. Experts suggest that a person with normal cognitive function should be able to name at least 18 in one minute. Ten or fewer is definitely abnormal. Numbers in between are questionable.
- Asking the patient to recall three objects as in the MMSE, but making the objects less common and attaching adjectives to them.

- Asking the patient to name and describe the function of a more complex object than used in the MMSE. For example, instead of a pen, use typewriter.
- Using a ten-word list with each word on a separate card. The examiner shows one card at a time and has the patient repeat each word individually, and then asks the patient to recite as many words as are recalled. A “normal” score is a recall of 5-6 words. The cards are then shuffled and the process repeated, with a “normal” result of 7-8 words recalled. Another shuffle and repeat can be performed, and people with no impairment usually recall 9-10 words at this point. While memory-impaired patients do learn across the trials, the improvement is much less than in those with no deficits.
- Expanding on the previous test 15-20 minutes later, asking the patient to name as many of the words as can be recalled. The number of correct recalls is typically close to the score on the third trial above. Finally, the examiner can show twenty cards that include the first 10, asking the patient to identify which were reviewed before. A normal result is 100% recognition of the words.

NEUROPSYCHOLOGICAL TESTING

Neuropsychological testing is the most definitive standard for diagnosis of early dementia. Such testing may be especially useful in patients who present early in the disease process, when the usual brief cognitive tests discussed above may lack sufficient sensitivity and specificity for diagnosis. It can also be helpful when dementia and depression are difficult to separate, or when atypical symptoms are present. In addition, clearer identification of specific cognitive deficits may be helpful in designing individualized coping strategies and behavior management.

Performance on neuropsychological testing is influenced by many factors, including education, cultural background, and co-morbid illnesses. A referral source with special expertise in dementia evaluation is particularly helpful when questions about such influences arise.

We are likely to use neuropsychological testing more often in the future, as patients, families, and physicians increasingly appreciate the benefits of early diagnosis and treatment for dementia. Currently, referral for neuropsychological testing should be considered when:

1. MMSE or other cognitive assessment is normal, but a family member expresses concerns
2. Patient has an unusually high or low educational status, literacy level, or intelligence
3. Patient is from a minority racial or ethnic background
4. MMSE is abnormal, but the functional assessment is normal

DIAGNOSIS “OVER TIME”

It may be difficult to be certain about the diagnosis of dementia in the early stages, and even the results of neuropsychological testing may be ambiguous. A clearer picture often emerges over time with repeated assessments. The primary care physician is in an ideal position for follow-up appointments that can include updated functional assessments and cognitive evaluation, making progression of disease much easier to identify.

REFERRAL TO SPECIALISTS

Referral to a clinician with dementia expertise (geriatrician, neurologist, or psychiatrist) should be considered in patients with any of the following:

- Age less than 65
- Atypical presentation or unclear diagnosis
- Rapid progression or deterioration
- Strong family history of dementia
- Any focal neurological symptoms or signs, including movement disorders
- Gait disturbance or urinary incontinence in the early stages of dementia,
- Prominent language symptoms or personality change

Referral is also indicated when the primary care physician does not feel comfortable with evaluation or management, or if the patient or family strongly desire consultation.

STAGING DEMENTIA

Clinical Diagnosis – Differential Diagnosis

Dementia can be broadly defined as a syndrome in which memory loss is accompanied by acquired impairment in at least one other cognitive domain, including the areas of language, motor function, personality, reasoning, and executive function (ability to plan and organize). Formal diagnostic criteria for dementia can be found in the Diagnostic and Statistical Manual of Mental Disorders.

Criteria for the two most common types of dementia can be found in the NINCDS-ADRDA for Alzheimer’s and NINDS-AIREN for vascular dementia.

Alzheimer’s <http://neurology.org/cgi/content/abstract/34/7/939>

Vascular dementia <http://neurology.org/cgi/content/abstract/43/2/250>

Identifying dementia is usually of greater importance to the primary care physician than differentiating the precise type and cause of the disease. By far, most cases of dementia the primary care clinician sees will be caused by Alzheimer's disease, either alone or in combination with another underlying cause like vascular dementia.

But in highly unusual cases, the sole source of dementia will be found to be a reversible condition, and somewhat more commonly, such a condition will coexist with Alzheimer's. Those disorders should be recognized and treated separately, even when Alzheimer's or another irreversible disease is present. Practitioners should know that truly reversible dementias are quite rare, especially in those over 65 in the primary care setting, with one meta-analysis estimating that less than 1% of cases of dementia have causes that lead to even partial reversibility (Clarfield MA, 2003).

Mild Cognitive Impairment vs. Dementia

In addition to knowing the difference between signs of dementia and changes that relate to normal aging, we need to be able to distinguish dementia from mild cognitive impairment (MCI).

Signs of Normal Aging Compared with Signs of Dementia

NORMAL AGING	DEMENTIA
Occasional short-term memory lapses (lost details can be restored by prompts)	Increasing short-term memory problems that get in the way of daily living (unresponsive to prompts because new memories are not being formed and cannot be retrieved)
Awareness of memory lapses	No awareness of memory problems Often needs reminders about appointments, medication schedule, etc.
Forgetting where you left the car keys	Forgetting what car keys are for
Occasionally misplacing items	Frequently misplacing items Leaving things in unusual places (e.g., milk in the breadbox)
Occasionally forgetting a word	Frequent inability to come up with words, communicate clearly, understand what is being said
Forgetting someone's name	Difficulty identifying a close friend or relative
Taking longer to perform tasks	Inability to perform familiar tasks
Taking longer to solve problems	Problems with abstract thinking

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	<i>Additional symptoms that should be recognized as possibly signs of dementia:</i>
	Withdrawal, loss of interest
	Mood and behavior changes
	Decreased ability to make good judgments
	Trouble remembering the date, time or place

The diagnosis of MCI recognizes that beyond a certain point, cognitive changes in aging individuals should not be considered normal, even when they do not meet all the accepted criteria for dementia.

A patient with MCI typically reports problems with short-term memory – such as not remembering the names of new people, not recalling the flow of a conversation, or misplacing an object. While these problems are seen in dementia, MCI presents clear differences. Significant among these is the likelihood that the patient will be the one to complain of the problem, something that is rarely true in cases of dementia, even in the early stage. Corroboration from another informant, however, should be taken as a sign that the patient has MCI rather than memory changes associated with normal aging. In addition, the patient:

- Performs poorly on formal memory tests, even in comparison to people of comparable age and education
- Shows normal general cognitive functions otherwise
- Experiences no interference with the activities of daily living and does not require added assistance in these areas beyond the previous level of need

As in the case of Alzheimer’s and related disorders, physicians should be careful to evaluate for coexisting or confounding depression. See the information about depression in the Depression and Dementia section that follows in this module.

MCI may be a transitional stage. It is estimated that people diagnosed with MCI will progress to Alzheimer’s at a rate of 10-15% per year as opposed to 1-2% in a healthy control group. But the cognitive changes found in MCI may never progress to clear-cut dementia in some cases. In light of the high conversion rate of MCI to Alzheimer’s, it is especially important to recall that when signs that suggest dementia are present, reassessment may be needed in order to make a diagnosis over time, discussed above.

Delirium and Dementia

Delirium represents the acute or subacute impairment of brain function due to the effects of physical illness. The Diagnostic and Statistical Manual provides criteria for delirium.

Delirium occurs with increasing frequency in advancing age, and dementia is a significant underlying risk factor for the development of delirium. In fact, the development of delirium may be the first sign of dementia in an elderly patient. In addition, delirium may be confused with dementia, especially in milder forms of delirium, when acute onset is not apparent. The chart below describes key differences that can help distinguish between the two:

	Delirium	Dementia
Onset	Acute or subacute	Gradual, insidious
Reversibility	Reversible	Irreversible; Progressive
Orientation	Disoriented	Not impaired (until advanced)
Consciousness	Fluctuates; Clouded	Intact (until advanced)
Attention	Impaired	Normal (until advanced)
Memory	Confused	Short-term losses
Cognitive deficits	Variable	Consistent
Psychomotor status	Hyperactive or hypoactive	Normal (until advanced)

Subacute delirium is more common in the elderly than in any other age group. This subacute presentation can easily cause it to be confused with dementia. Metabolic disturbances and drug effects are the most common causes of subacute delirium in the elderly population.

It is important for the primary care physician to be able to identify delirium as an acute response to a medical problem that requires urgent treatment. The clinician should also recognize that delirium can accompany dementia, and effective treatment for the underlying cause of delirium may still leave dementia that needs to be addressed separately. Delirium can also be a warning sign for dementia, and should be a trigger for the physician to investigate possible dementia.

⌘ Any patient with delirium should be evaluated for underlying dementia when stable.

Depression and Dementia

Depression in an older patient can be easily mistaken for dementia, and vice versa. Many of the early presenting symptoms and signs are similar in both conditions: apathy, neglect of self-care, memory loss, and other impaired cognitive functioning. A personal or family history of depression may be helpful in recognizing depression; a first-ever depression after age 60 is unusual in the absence of a clear precipitant like trauma or grief. However, there are also important differences that can help the clinician distinguish between depression and dementia as shown in the chart below.

	Depression	Dementia
Onset	More discrete onset	Insidious
Mood	Low most of the day, Sadness may be masked by physical symptoms	Fluctuates without pattern; Mood changes in addition to depression are common
Physical symptoms	May be prominent – aches and pains, GI symptoms, headache, etc.	Uncommon
Cognitive loss	Fluctuates	Stable and progressive
Memory loss	Apathy – short and long-term both affected	Short-term memory much more impaired
Presentation	Patient likely to present concerns	Relative or friend likely to present concerns

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Patient perception	Complains about memory loss	Unaware of memory loss; Underestimates problems
Answers to Questions	“Don’t know;” Incomplete answers	Inappropriate or “near miss”
Effort on tasks	Low	Normal

The Geriatric Depression Scale is a valuable screening tool for depression in the elderly.

Geriatric Depression Scale (Short Form)

Choose the best answer for how you felt the past week:

Are you basically satisfied with your life?	Yes	No*
Have you dropped many of your activities and interests?	Yes*	No
Do you often feel that your life is empty?	Yes*	No
Do you often get bored?	Yes*	No
Are you in good spirits most of the time?	Yes	No*
Are you afraid that something bad is going to happen to you?	Yes*	No
Do you feel happy most of the time?	Yes	No*
Do you often feel helpless?	Yes*	No
Do you prefer to stay at home rather than going out and doing new things?	Yes*	No
Do you feel you have more problems with memory than most?	Yes*	No
Do you think it is wonderful to be alive now?	Yes	No*
Do you feel pretty worthless the way you are now?	Yes*	No
Do you feel full of energy?	Yes	No*
Do you feel your situation is hopeless?	Yes*	No
Do you think most people are better off than you are?	Yes*	No

Each answer marked by an asterisk counts as one point.

(Public Domain)

The GDS has 15 yes-or-no questions on a form designed to be self-administered and it takes only 5-10 minutes to complete. A score between 5 and 9 suggests

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depression, while a score greater than 9 correlates very strongly to depression. Further assessment is needed to confirm the diagnosis if the GDS is positive.

The primary care physician needs to be able to identify treatable depression in older patients. Treatment with antidepressants may alleviate all of the symptoms that mimic dementia, but the clinician should know that depression is also a common co-morbidity of Alzheimer's. Depression is a recognized risk factor for dementia as well; therefore, underlying dementia should be suspected in all elderly patients with depression. In cases where dementia and depression coexist, it is important to identify and treat both.

⌘ Any patient with depression should be evaluated for underlying dementia.

Major Types of Dementia

Although dementia has many causes, the three major causes account for almost all of the cases seen and managed by primary care physicians (see referral criteria above): Alzheimer's disease; vascular dementia; and dementia with Lewy bodies.

Alzheimer's Disease

Alzheimer's disease should always be suspected when signs of dementia are identified. It is the predominant cause of dementia and often coexists with other disorders that contribute to the dementia syndrome. Key elements of Alzheimer's dementia are:

- Insidious onset
- Progressive course
- Impaired memory (both in recalling previously learned information and in learning new information)
- Impairments in one or more of the areas of :
 - Language
 - Orientation
 - Ability to carry out motor activities (apraxia)
 - Ability to recognize or identify objects (agnosia)
 - Executive function (ability to plan and organize, to abstract – this may be subtle)

A patient may also be apathetic and emotionally withdrawn.

Vascular Dementia

The symptoms of vascular dementia are not easily distinguishable from the symptoms of Alzheimer's disease, and a significant number of individuals who have dementia from cerebrovascular causes also have Alzheimer's. There are differences that can be identified, however:

- Onset can be abrupt, but is more often subtle
- Progression may be stepwise
- Focal neurological signs may be present
- Cognitive deficits correlate with lesions on imaging
- Gait disturbances and urinary incontinence may be present
- Risk is higher in patients with hypertension, diabetes, and coronary artery disease

Most significantly, vascular dementia has a temporal association between the development of cognitive impairment and either clinical or imaging evidence of effects of vascular disease.

However, dementia without sudden onset often goes undiagnosed following a CVA (cerebrovascular accident, or stroke). In many studies, the rate of dementia after a CVA is around 30%. And studies have demonstrated that many people diagnosed with vascular dementia also have clear evidence of Alzheimer's disease at autopsy.

Dementia with Lewy Bodies (DLB) / Dementia from Parkinson's Disease

It is unclear whether dementia with Lewy bodies and dementia associated with Parkinson's disease, which has many features similar to Alzheimer's, are two separate entities or simply variants of one type. Like Alzheimer's, DLB is insidious in onset and progressive, but it may be distinguished by:

- Fluctuations in cognitive function with varying levels of alertness and attention
- Visual hallucinations that may become evident early in the course of disease
- Parkinsonian motor features, especially rigidity and bradykinesia
- Nighttime behavioral disturbances and daytime drowsiness
- Less prominent memory loss early in the course of the illness
- More prominent executive dysfunction early in the course of the illness
- Sensitivity to neuroleptic side effects

These three types of dementia – Alzheimer's disease, vascular dementia, and dementia with Lewy Bodies – have significant overlap in clinical presentation and

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treatment: cholinesterase inhibitors are valuable in slowing the progression of all three and control of vascular risk factors is important in all three. The clinical importance of making a clear distinction among them has been overemphasized.

⌘ Identification of dementia is far more important than precise identification of its cause.

TABLE A
The Mini-Mental Status Exam
 Standard version – Folstein, Folstein, McHugh, 1975
 (To be completed by a trained clinician)

Patient Name: _____

Date: _____ **Time:** _____

Birth Date: _____

Sex:

- Male
- Female

Education (years): _____

Race:

- Caucasian
- Black
- Hispanic
- Asian
- Other

Orientation Questions:

Question	Right	Wrong
1. What is today's date?		
2. What is the month?		
3. What is the year?		
4. What day of the week is today?		
5. What season is it?		
6. What is the name of this clinic (place)?		
7. What floor are we on?		
8. What city are we in?		
9. What county are we in?		
10. What state are we in?		

Immediate Recall: Ask the subject if you may test his/her memory. Then say "ball," "flag," "tree" clearly and slowly, about one second for each. After you have said all three words, ask him/her to repeat them. The first repetition determines the score (0-3), but keep saying them until he/she can repeat all three, up to six tries. If he/she does not eventually learn all three, recall cannot be meaningfully tested:

11. Ball		
12. Flag		
13. Tree		
Note the Number of Trials: _____		

Attention:

- A. Ask the subject to begin with 100 and count backwards by 7. Stop after 5 subtractions. Score the correct subtractions.

14. "93"		
15. "86"		
16. "79"		

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17. "72"		
18. "65"		
Serial 7's Total: _____		

Patient Name: _____

B. Ask the subject to spell the word "WORLD" backwards. The score is the number of letters in the correct position. For example, "DLORW" is 3, "LROWD" is 0.

Question	Right	Wrong
19. "D"		
20. "L"		
21. "R"		
22. "O"		
23. "W"		
"DLROW" Total: _____		Greater Score A or B:

Delayed Verbal Recall: Ask the subject to recall the three words you previously asked him/her to remember.

24. BALL?		
25. FLAG?		
26. TREE?		
RECALL: _____		

Naming: Show the subject a wrist watch and ask him/her what it is. Repeat for pencil.

27. WATCH		
28. PENCIL		
29. REPITON		

Three Stage Command: Give the subject a plain piece of paper and say, "Take the paper in your hand, fold in half, and put it on the floor."

30. TAKES		
31. FOLDS		
32. PUTS		

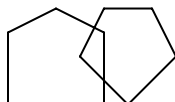
Reading: Hold up the card reading, "Close your eyes", so the subject can see it clearly. Ask him/her to read and do what it says. Score correctly only if the subject actually closes his/her eyes.

33. CLOSES EYES		
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Writing: give subject a piece of paper and him/her to write 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.

34. SENTENCE LANGUAGE		
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Pentagons: Ask the subject to draw they the two pentagons as they appear on the paper.



35. PENTAGONS		
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MMSE

Patient Name: _____

Calculations:

Total the number of correct responses: _____

(MMSE maximum score = 30)

24-30 normal, depending on age, education and complaints

20-23 mild

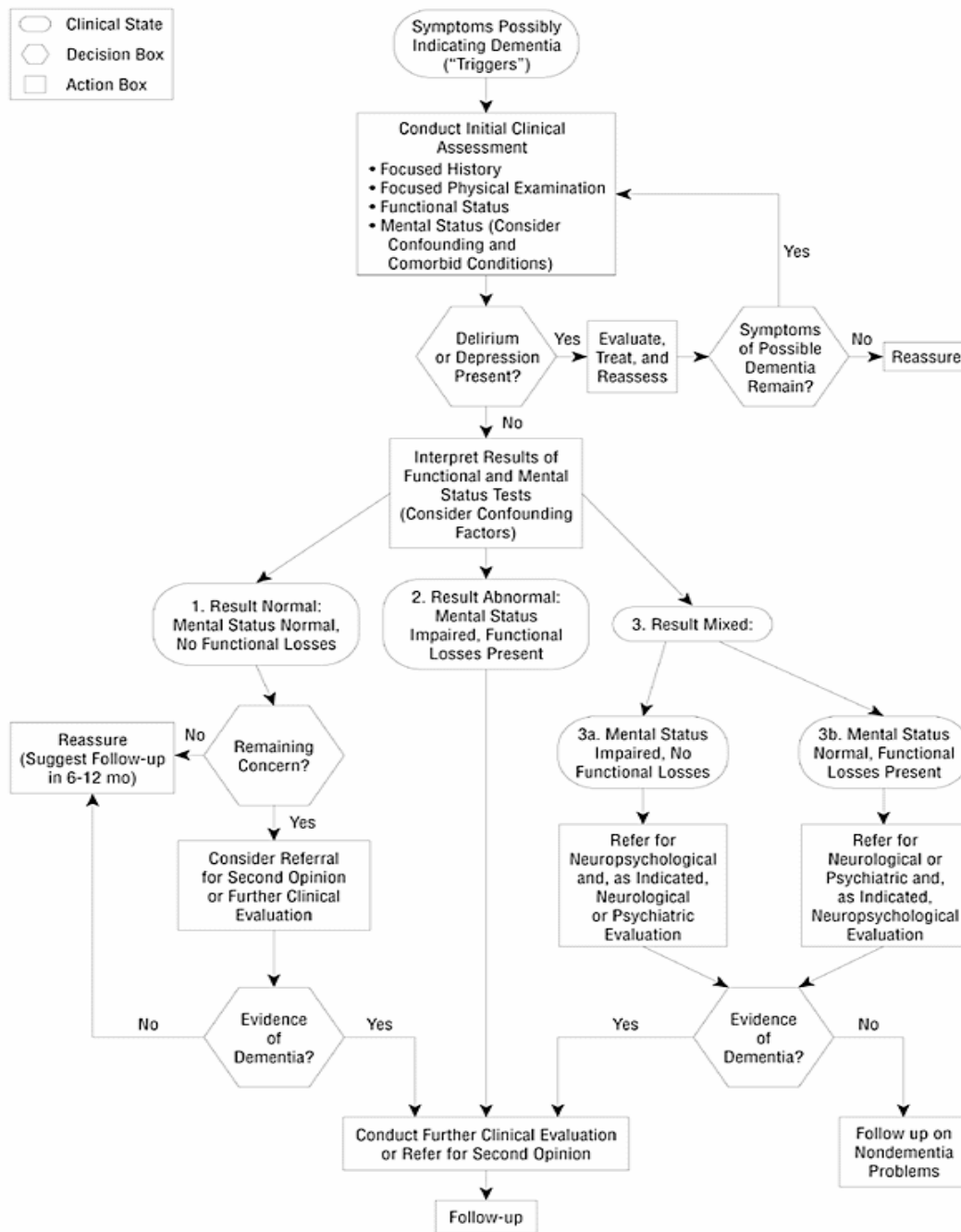
10-19 moderate

1- 9 severe

0 profound

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TABLE B
Flow Chart for Recognition and Initial Assessment of
Alzheimer's Disease and Related Dementias¹



¹ Source: Agency for Health Care Policy and Research, 1996.

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