National Institute on Aging/Alzheimer's Association

Diagnostic Guidelines for Alzheimer's Disease

FREQUENTLY ASKED QUESTIONS FOR CLINICIANS

1. What are the main differences between the 1984 diagnostic criteria for Alzheimer's disease and the new guidelines?

The new guidelines differ from the 1984 diagnostic criteria in a few key ways. They:

- Recognize that Alzheimer's disease progresses on a spectrum with three stages—an early, preclinical stage with no symptoms; a middle stage of mild cognitive impairment; and a final stage marked by symptoms of dementia. The 1984 criteria addressed only one stage of disease—the final stage of dementia.
- Expand the criteria for Alzheimer's dementia beyond memory loss as the first or only major symptom. They recognize that other aspects of cognition, such as word-finding ability or judgment, may become impaired first. The 1984 criteria focused on memory loss as the central emerging characteristic of Alzheimer's dementia.
- Reflect a better understanding of the distinctions and associations between Alzheimer's and non-Alzheimer's dementias, as well as between Alzheimer's and disorders that may influence its development, such as vascular disease. In 1984, these relationships were not well recognized or understood.
- Recognize the potential use of biomarkers—indicators of underlying brain disease—to diagnose Alzheimer's disease. However, the guidelines state that biomarkers are almost exclusively to be used in research rather than in a clinical setting. These biomarkers did not exist when the original criteria were developed in 1984, so confirmation of the diagnosis was possible only through autopsy after death.

2. Why were the diagnostic criteria revised and who led the effort?

The diagnostic criteria for Alzheimer's disease were revised to reflect a deeper understanding of the disease. During the past 27 years, scientists have learned much about the physical brain changes of Alzheimer's, how the changes progress over time, and how they correspond to clinical symptoms. More specifically, researchers have learned that Alzheimer's pathology begins years before clinical symptoms appear, and that this pathology has an ordered sequence. Exactly how and when specific amyloid and neurodegenerative pathology correlates to clinical symptoms continues to be studied.

Alzheimer's Disease Education & Referral (ADEAR) Center
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For more information, see: *www.nia.nih.gov/Alzheimers/Publications/ADProgress2009/Advances/Deciphering/normal.htm*

The revised criteria spell out new diagnostic approaches for clinicians, similar to the ones used now but with some refinements, and provide scientists with the most advanced criteria for examining Alzheimer's and potential treatments in a research setting.

The new guidelines were developed by expert panels convened by the National Institute on Aging, part of the National Institutes of Health, and the Alzheimer's Association, the leading voluntary health organization in Alzheimer's care, support, and research.

3. Where are the new diagnostic criteria published?

The new diagnostic criteria for Alzheimer's disease can be found in the April 19, 2011, issue of *Alzheimer's & Dementia: the Journal of the Alzheimer's Association*, a peer-reviewed medical journal. To view the papers outlining the new guidelines, go to: *www.alz.org/research/diagnostic_criteria*.

4. How is Alzheimer's disease defined in the updated diagnostic guidelines?

In summary, the updated diagnostic guidelines describe three stages of Alzheimer's disease:

- *Preclinical*—Brain changes, including amyloid buildup and other nerve cell changes, may already be in progress, but significant clinical symptoms are not yet evident.
- *Mild cognitive impairment (MCI)*—A stage marked by symptoms of memory and/or other thinking problems that are greater than normal for a person's age and education, but that do not interfere with his or her independence. People with MCI may or may not progress to Alzheimer's dementia.
- *Alzheimer's dementia*—The final stage of the disease in which symptoms of Alzheimer's, such as memory loss, word-finding difficulties, and visual/spatial problems, are significant enough to impair a person's ability to function independently.

5. When and how should healthcare professionals apply the revised guidelines in clinical practice?

The core clinical criteria for the diagnosis of mild cognitive impairment (MCI) due to Alzheimer's disease and Alzheimer's dementia can be applied to clinical practice immediately. The new guidelines for the diagnosis of preclinical Alzheimer's are for research settings only; further research is needed to refine, validate, and standardize biomarkers before they are ready for general clinical practice. However, fluid and imaging biomarker tests may in some cases supplement standard clinical tests in specialized clinical settings, such as research centers, to determine possible causes of MCI and to increase or decrease the certainty of an Alzheimer's dementia diagnosis.

6. How do the new guidelines change the way clinicians diagnose mild cognitive impairment or Alzheimer's disease? Should they still use the same tests and screening tools? Should they use any new tests or screening tools?

Clinicians should continue to use the many validated neuropsychological tests currently available. These include formal tests that assess various cognitive functions—episodic memory, executive function, language, visual and spatial skills, and attention. Interviews with the person as well as a family member, friend, or caregiver about changes in the person's thinking skills are also helpful.

Clinicians should also consider augmenting the evaluation process they have been using. To learn more about a variety of simple, informal techniques that can be used to assess cognitive function, go to: *www.alzheimersanddementia.com/article/S1552-5260(11)00104-X/fulltext*.

If a problem is suspected, more extensive evaluation by a specialist should be recommended to the patient and family. The Alzheimer's Association, Alzheimer's Foundation of America, local Area Agency on Aging offices, and a variety of organizations offer information and help with planning for the future.

7. What are the core clinical criteria for the diagnosis of mild cognitive impairment?

Mild cognitive impairment (MCI) refers to the symptomatic, pre-dementia phase of the disease. It should be noted, however, that MCI may be due to causes other than Alzheimer's disease. A diagnosis of MCI requires all of the following:

- concern about a change in cognition relative to previous functioning
- impairment of one or more cognitive functions, like memory and problem solving, that is greater than expected for the person's age and education. (Memory is the function most commonly impaired among people who progress from MCI to Alzheimer's dementia.)
- preserved ability to function independently in daily life, though some complex tasks may be more difficult than before
- no dementia

Clinicians should obtain long-term assessments of cognition whenever possible to gain evidence of progressive decline. To determine that MCI is due to Alzheimer's disease, a doctor must rule out other brain diseases or other causes—such as medications, depression, or major life changes—that could account for cognitive decline.

8. How should clinicians approach the question of preclinical Alzheimer's with patients?

Preclinical Alzheimer's disease is an experimental concept at this time. While imaging and biomarker studies strongly indicate a preclinical phase for the disease, it is not yet

possible to predict which cognitively healthy individuals will and will not progress to MCI or dementia. Researchers hope to develop a biomarker profile that will identify individuals most likely to develop Alzheimer's dementia and benefit from early treatments when they become available.

9. Should treatment approaches change as a result of the revised guidelines?

The new criteria are for research and diagnostic purposes only. They do not affect treatment approaches. Scientists hope that diagnostic research will aid the search for effective disease-modifying therapies through better understanding of the biological basis for the disease. For current treatment guidelines, see: *www.nia.nih.gov/Alzheimers/Publications/ADProgress2009/Primer/treated.htm*.

10. What is the role of genetic testing in the revised guidelines?

A rare type of familial Alzheimer's disease, called Early-Onset Alzheimer's Disease (EOAD), is caused by mutations in the amyloid precursor protein, presenilin 1, or presenilin 2 genes. A person who inherits any of these mutations from a parent will almost surely develop Alzheimer's dementia before age 65. Genetic testing for the disease is common in families with a history of EOAD.

The major genetic risk factor for the more common, sporadic form of the disease, or Late-Onset Alzheimer's Disease (LOAD), is the ε4 allele of the APOE gene. But carrying this allele by itself does not mean a person has or will develop Alzheimer's dementia, so genetic testing for APOE ε4 is not recommended outside of a research setting.

11. Why are some of the guidelines limited to research settings?

Some of the new guidelines—specifically, those for using biomarkers to assess preclinical Alzheimer's disease and to increase the certainty of diagnoses of MCI and dementia due to Alzheimer's disease—are to be used only for research. Before doctors can use these guidelines in clinical practice, more research is needed to make sure biomarkers can help predict who will or will not develop Alzheimer's dementia. Biomarker tests also must be standardized to ensure they can be measured correctly and consistently in all clinical settings.

12. How will these guidelines be reviewed and updated in the future?

As results become available, future panels will consider emerging technologies and advances in the understanding of biomarkers and the disease process itself. The diagnostic framework was intended to be flexible enough to incorporate new scientific findings. The Alzheimer's Disease Neuroimaging Initiative (*www.adni-info.org*), funded in part by NIA, is actively researching the field of preclinical disease and biomarkers.

For more information about Alzheimer's clinical trials, visit NIA's ADEAR Center at *www.nia.nih.gov/Alzheimers* or call 1-800-438-4380. More information about clinical trials is available at: *www.ClinicalTrials.gov*. Also see **Participating in Alzheimer's Disease Clinical Trials and Studies** at: *www.nia.nih.gov/Alzheimers/Publications/trials-studies.htm*.