

Alzheimer's Association:

Trends, Biomarkers, and New Approaches to Diagnosis

The latest data report from the association highlights the current and future burden of AD and outlines proposed new approaches to diagnosis.

An estimated 5.2 million Americans of all ages currently have Alzheimer's disease, about five million of whom are over age 65. As the population ages, by 2050, the number of people age 65 and older with Alzheimer's disease may increase to a projected 13.8 million. In 2031, when the first wave of baby boomers reaches age 85, more than three million people age 85 and older are projected to have Alzheimer's. Those are findings from the Alzheimer's Association in their "2013 Alzheimer's Disease Facts and Figures" report, released in March.

The sixth leading cause of death in the US and the fifth leading cause among those age 65 or older, Alzheimer's is most often diagnosed by a primary care physician, the Association reports. Given that some cases of dementia go undiagnosed and many more go unclassified, the Alzheimer's Association in conjunction with the National Institute on Aging are proposing new criteria and guidelines that update the diagnostic criteria and guidelines published in 1984 by the Alzheimer's Association and the National Institute of Neurological Disorders and Stroke.

Last year, the NIA and the Alzheimer's Association proposed new guidelines intended to help pathologists describe and categorize the brain changes associated with Alzheimer's disease and other dementias.

PROPOSED GUIDELINES

In its new report, the Alzheimer's Association highlights difference between the 1984 diagnostic criteria and guide-

lines, which primarily relied on a physician's clinical judgment about the cause of an individual's symptoms based on reports from the individual, family members and friends; results of cognitive tests; and general neurological assessment. The new criteria and guidelines incorporate two notable changes, the Association says:

1.) They identify three stages of Alzheimer's disease, with the first occurring before symptoms such as memory loss develop. In contrast, for Alzheimer's disease to be diagnosed using the 1984 criteria, memory loss and a decline in thinking abilities severe enough to affect daily life must have already occurred.

2.) They incorporate biomarker tests. A biomarker is a biological factor that can be measured to indicate the presence or absence of disease, or the risk of developing a disease. For example, blood glucose level is a biomarker of diabetes, and cholesterol level is a biomarker of heart disease risk. Levels of certain proteins in fluid (for example, levels of beta-amyloid and tau in the cerebrospinal fluid and blood) are among several factors being studied as possible biomarkers for Alzheimer's.

THREE STAGES OF ALZHEIMER'S DISEASE

The New Criteria and Guidelines proposes three stages of Alzheimer's disease: Preclinical Alzheimer's disease; Mild cognitive impairment (MCI) due to Alzheimer's disease, and dementia due to Alzheimer's disease. These new stages

ALZHEIMER'S FACTS

68%. Rate of increase in deaths attributed to Alzheimer's disease between 2000 and 2010 in the US.

16%. Rate of increase in deaths attributable to heart disease—the number one cause of death in the US.

5-15%. Proportion of all deaths in older people that can be attributed to Alzheimer's disease.

4-8 years. Average time of survival among people age 65 and older after receiving a diagnosis of Alzheimer's disease.

66%. Percentage of individuals who die of dementia in nursing homes.

20%. Percentage of cancer patients who die in nursing homes.

28%. Percentage of people dying from all other conditions in nursing homes.

17.5 billion. Hours of unpaid care provided by community caregivers in 2012.

15.4 million. Number of family and other unpaid caregivers of people with Alzheimer's disease in the US.

emerged in part from the proposal in the 2011 criteria that Alzheimer's disease begins before the development of symptoms and acknowledgement that new technologies may be able to identify brain changes that precede the development of symptoms. The new criteria designate an individual with these early brain changes as having preclinical Alzheimer's disease or MCI due to Alzheimer's. Dementia due to Alzheimer's would encompass all stages of Alzheimer's disease commonly described today, from mild to moderate to severe, the Association says. They further delineate the stages of Alzheimer's.

Preclinical Alzheimer's disease: In this stage, individuals have measurable changes in the brain, cerebrospinal fluid and/or blood (biomarkers) that indicate the earliest signs of disease, but they have not yet developed symptoms such as memory loss. This preclinical or presymptomatic stage reflects current thinking that Alzheimer's-related brain changes may begin 20 years or more before symptoms occur. Although the new criteria and guidelines identify a modern diagnosis of preclinical disease as a stage of Alzheimer's, they do not establish diagnostic criteria that doctors can use now. Rather, they state that additional research on biomarker tests is needed before this stage of Alzheimer's can be diagnosed.

MCI due to Alzheimer's disease: Individuals with MCI have

mild but measurable changes in thinking abilities that are noticeable to the person affected and to family members and friends, but that do not affect the individual's ability to carry out everyday activities. Studies indicate that as many as 10 to 20 percent of people age 65 or older have MCI. As many as 15 percent of people whose MCI symptoms cause them enough concern to contact their doctor's office for an exam go on to develop dementia each year. Nearly half of all people who have visited a doctor about MCI symptoms will develop dementia in three or four years. When MCI is identified through community sampling, in which individuals in a community who meet certain criteria are assessed regardless of whether they have memory or cognitive complaints, the estimated rate of progression to Alzheimer's is slightly lower—up to 10 percent per year. Further cognitive decline is more likely among individuals whose MCI involves memory problems than among those whose MCI does not involve memory problems. Over one year, most individuals with MCI who are identified through community sampling remain cognitively stable. Some, primarily those without memory problems, experience an improvement in cognition or revert to normal cognitive status. It is unclear why some people with MCI develop dementia and others do not. When an individual with MCI goes on to develop dementia, many scientists believe the MCI is actually an early stage of the particular form of dementia, rather than a separate condition. Once accurate biomarker tests for Alzheimer's have been identified, the new criteria and guidelines recommend biomarker testing for people with MCI to learn whether they have brain changes that put them at high risk of developing Alzheimer's disease and other dementias. If it can be shown that changes in the brain, cerebrospinal fluid and/or blood are caused by physiologic processes associated with Alzheimer's, the new criteria and guidelines recommend a diagnosis of MCI due to Alzheimer's disease.

Dementia due to Alzheimer's disease: This stage is characterized by memory, thinking and behavioral symptoms that impair a person's ability to function in daily life and that are caused by Alzheimer's disease-related brain changes.

THE POTENTIAL OF BIOMARKERS

Some biomarkers show the level of beta-amyloid accumulation in the brain, while others show neurons in the brain are injured or degenerating, the Alzheimer's Association observes. Because disease-modifying therapies are anticipated to be most effective when administered during the preclinical and MCI stages of the disease, biomarker based tests may become increasingly more useful in the clinical setting. Biomarker tests also may be utilized to monitor the effects of treatment. Additional research is needed to determine which test offers the greatest utility and in which patients. ■