TABLE **1**

Common Causes of Dementia

Cause	Brain changes
Alzheimer's disease	Accumulation of the protein beta-amyloid outside neurons and twisted strands of the protein tau inside neurons are hallmarks. They are accompanied by the death of neurons and damage to brain tissue. Inflammation and atrophy of brain tissue are other changes.
Cerebrovascular disease	Blood vessels in the brain are damaged and/or brain tissue is injured from not receiving enough blood, oxygen or nutrients. People with these changes who develop dementia symptoms are said to have vascular dementia.
Frontotemporal degeneration (FTD)	Nerve cells in the front and temporal (side) lobes of the brain die and the lobes shrink. Upper layers of the cortex soften. Abnormal amounts or forms of tau or transactive response DNA-binding protein (TDP-43) are present.
Hippocampal sclerosis (HS)	HS is the shrinkage and hardening of tissue in the hippocampus of the brain. The hippocampus plays a key role in forming memories. HS brain changes are often accompanied by accumulation of the misfolded protein TDP-43.
Lewy body disease	Lewy bodies are abnormal aggregations (or clumps) of the protein alpha-synuclein in neurons. When they develop in a part of the brain called the cortex, dementia can result. This is called dementia with Lewy bodies or DLB.
Limbic-predominant age-related TDP-43 encephalopathy (LATE)	A protein called transactive response DNA-binding protein 43 (TDP-43) accumulates in the brain. TDP-43 is a naturally occurring protein that helps with nerve development. In LATE, it usually accumulates in parts of the brain involved in memory, emotion, behavior and mood (limbic system).
Mixed pathologies	When an individual shows the brain changes of more than one cause of dementia, "mixed pathologies" are considered the cause. When these pathologies result in dementia symptoms during life, the person is said to have mixed dementia or mixed etiology dementia.
Parkinson's disease (PD)	Clumps of the protein alpha-synuclein appear in an area deep in the brain called the substantia nigra. These clumps are thought to cause degeneration of the nerve cells that produce the chemical dopamine.[34] As PD progresses, alpha-synuclein can also accumulate in the cortex.

Percentage of dementia cases	Symptoms
Alzheimer's is the most common cause of dementia, accounting for an estimated 60% to 80% of cases. Most individuals also have the brain changes of one or more other causes of dementia.[25,26] This is called mixed pathologies, and if recognized during life is called mixed dementia.	Difficulty remembering recent conversations, names or events; apathy; and depression are often early symptoms. Communication problems, confusion, poor judgment and behavioral changes may occur next. Difficulty walking, speaking and swallowing are common in the late stages of the disease.
About 5% to 10% of individuals with dementia show evidence of vascular dementia alone.[25,26] However, it is more common as a mixed pathology, with most people living with dementia showing the brain changes of cerebrovascular disease and Alzheimer's disease.[25,26]	Slowed thoughts or impaired ability to make decisions, plan or organize may be the initial symptoms, but memory may also be affected. People with vascular dementia may become less emotional and have difficulty with motor function, especially slow gait and poor balance.
About 60% of people with FTD are ages 45 to 60.[27] In a systematic review, FTD accounted for about 3% of dementia cases in studies that included people 65 and older and about 10% of dementia cases in studies restricted to those younger than 65.[28]	Typical early symptoms include marked changes in personality and behavior and/or difficulty with producing or comprehending language. Unlike Alzheimer's, memory is typically spared in the early stages of disease.
HS is present in about 3% to 13% of people with dementia.[29] It often occurs with the brain changes of other causes of dementia. An estimated 0.4% to 2% of dementia cases are due to HS alone.[29]	The most pronounced symptom of HS is memory loss, and individuals are often misdiagnosed as having Alzheimer's disease. HS is a common cause of dementia in individuals age 85 or older.
About 5% of older individuals with dementia show evidence of DLB alone, but most people with DLB also have the brain changes of Alzheimer's disease.[30]	Early symptoms include sleep disturbances, well-formed visual hallucinations and visuospatial impairment. These symptoms may change dramatically throughout the day or from day to day. Problems with motor function (similar to Parkinson's disease) are common. Memory loss may occur at some point in the disease.
While the percentage of dementia cases caused by LATE is unknown, autopsy studies of more than 6,000 people found that 40% had the TDP-43 deposits characteristic of LATE, and that LATE was associated with deficits in memory and thinking in approximately 25% of the individuals.[31]	Symptoms are similar to those of Alzheimer's but begin at an older age (75 or older), are milder and worsen more slowly. Individuals initially have fewer cognitive and functional problems than individuals living with Alzheimer's.
More than 50% of people diagnosed with Alzheimer's dementia who were studied at Alzheimer's Disease Research Centers had mixed dementia.[26] In community-based studies, the percentage is considerably higher.[25] Mixed dementia is most common in people age 85 or older.[32,33]	Symptoms vary depending on the combination of brain changes present.
A systematic review found that 3.6% of dementia cases were due to PD and 24.5% of people with PD developed dementia.[35]	Problems with movement (slowness, rigidity, tremor and changes in gait) are common symptoms of PD. Cognitive symptoms may develop later in the disease, typically years after movement symptoms.

Prevalence Estimates

The prevalence numbers included in this report are based on estimates of how many people in the U.S. are living with Alzheimer's dementia; that is, the number of people living with the clinical symptoms described in the "Dementia Due to Alzheimer's Disease" (mild, moderate or severe) portion of the "Alzheimer's Disease Continuum" described in the Overview.

The estimate of 7.2 million older adults who have Alzheimer's dementia comes from a single longitudinal study in which participants were systematically evaluated and then re-evaluated on a regular basis; those who exhibited the clinical symptoms of Alzheimer's dementia were classified as having Alzheimer's dementia.[A2, 293] A major advantage of this approach is that it attempts to capture all individuals living with the condition and does not rely on the diagnosis of people living with Alzheimer's by the health care system, a process that has resulted in a substantial undercount (i.e., "underdiagnosis") of the Alzheimer's population. The disadvantage is that the longitudinal study is located in a single, small geographic area and may not be nationally representative (although the estimation process attempted to account for the demographics of the entire U.S. population). In the future, *Facts and Figures* could report estimates of Alzheimer's dementia prevalence from multiple longitudinal studies or using different symptom-based diagnostic criteria; these differences in criteria could result in different prevalence estimates from what we report here.

Almost all existing Alzheimer's dementia prevalence studies are based on the identification of clinical symptoms to classify an individual as having Alzheimer's dementia; they do not rely on the brain changes believed to be responsible for Alzheimer's disease across the continuum of the disease. As data sources, methods and scientific knowledge improve, estimates of prevalence may incorporate these brain changes using biomarkers. This addition could lead to very different prevalence estimates for a number of reasons, which are discussed below.

Estimated Prevalence of Dementia Due to Alzheimer's Disease Based on Biomarkers and Dementia Symptoms

Prevalence estimates of dementia due to Alzheimer's disease based on Alzheimer's brain changes, as well as overt clinical dementia symptoms, are likely to be lower than the 7.2 million figure reported here. This is because autopsy- and biomarker-based studies[25, 83, 295-297] indicate that some individuals counted as having Alzheimer's dementia based on symptoms do not have the biological brain changes defined as Alzheimer's disease; that is, their dementia is caused by something other than Alzheimer's disease. Both autopsy studies and clinical trials have found that 15% to 30% of individuals who met the criteria for clinical Alzheimer's dementia based on symptoms did not have Alzheimer's-related brain changes. Thus, these studies indicate that prevalence estimates using biomarkers of Alzheimer's disease could be up to 30% lower than prevalence estimates based only on symptoms. This would translate to roughly 5 million Americans age 65 and older being classified as having dementia due to Alzheimer's disease in 2025.

Estimated Prevalence of MCI Due to Alzheimer's Disease Based on Biomarkers and Mild Cognitive Symptoms

For decades, it has been recognized that all individuals with dementia pass through a precursor stage frequently referred to as mild cognitive impairment (MCI; see Overview). With the recent advent of biomarkers that detect the brain changes believed to characterize Alzheimer's disease, it may now be possible to determine which individuals diagnosed with MCI have MCI due to Alzheimer's disease. The number and proportion of older adults who have MCI due to Alzheimer's disease are currently difficult to estimate because they require studies with both population-based prevalence measures of MCI and tests of Alzheimer's biomarkers, and this line of research is in its infancy. Furthermore, there is variation across studies in both the threshold of cognitive impairment required for an MCI diagnosis and the level of biomarker burden that defines the presence of Alzheimer's disease. However, we can roughly estimate this prevalence indirectly using multiple data sources. A systematic review of more than 30 studies of all-cause MCI reported that about 17% of people age 65 and older had MCI.[298] The HRS HCAP study more recently estimated the prevalence of MCI in people age 65 and older to be 22%.[173] Meanwhile, studies assessing biomarkers for Alzheimer's disease with PET scans have reported that about half of people with MCI have Alzheimer's-related brain changes.[299, 300] Therefore, roughly 8% to 11% of the 65 million Americans who are age 65 and older in 2025 — or approximately 5 to 7 million older Americans — may have MCI due to Alzheimer's disease.[301] This estimate needs to be refined with population-based studies involving biomarkers and more precise estimates from narrower age ranges.