

## 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 on pages 10-11 of the Overview.

The estimate of 6.9 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.<sup>A2, 241</sup>

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.<sup>A3, 160</sup>

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.

### Prevalence Estimates 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 6.9 million figure reported here. This is because autopsy- and biomarker-based studies<sup>21, 79, 243-245</sup> 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 meet the criteria for clinical Alzheimer's dementia based on symptoms did not have Alzheimer's-related brain changes. Thus, these studies indicate that 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 4.8 million Americans age 65 and older being classified as having dementia due to Alzheimer's disease in 2024.<sup>A3, 160</sup>

### Prevalence Estimates 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, page 10). 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.<sup>51</sup> The HRS HCAP study more recently estimated the prevalence of MCI in people age 65 and older to be 22%.<sup>160</sup> 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.<sup>246, 247</sup> Therefore, roughly 8% to 11% of the 63 million Americans who are age 65 and older in 2024 — or approximately 5 to 7 million older Americans — may have MCI due to Alzheimer's disease.<sup>248</sup> This broad prevalence estimate needs to be refined with population-based studies involving biomarkers and more precise estimates from narrower age ranges.

### **Prevalence Estimates of Alzheimer's Disease Based on Biomarkers and any Cognitive Symptoms (MCI or Dementia)**

Combining the estimates of the prevalence of dementia due to Alzheimer's disease and the prevalence of MCI due to Alzheimer's disease provides an estimate of people living with the brain changes of Alzheimer's disease and some form of cognitive impairment. This estimate would include older adults with the earliest detectable stages of cognitive impairment who have the brain changes of Alzheimer's but may or may not have the overt symptoms of dementia that interfere with their ability to carry out everyday activities. Combining the estimates of roughly 4.8 million Americans age 65 and older with dementia due to Alzheimer's disease based on Alzheimer's brain changes and the 5 to 7 million older Americans with MCI due to Alzheimer's disease translates to approximately 10 to 12 million older Americans with Alzheimer's disease and some form of cognitive impairment in 2024. Furthermore, because MCI develops years before dementia onset and can affect individuals younger than 65, there are likely more than 5 to 7 million people of any age with MCI due to Alzheimer's disease, and thus the 10 to 12 million estimate could be even higher if we consider Americans of all ages, not just those 65 or older.

### **Prevalence Estimates of Alzheimer's Disease Across the Entire Cognitive Spectrum**

Finally, as measurements of the brain changes of Alzheimer's disease become more widely available in research, we will be able to estimate how many people have Alzheimer's disease regardless of the presence or absence of dementia or any form of cognitive impairment. The total number of people living with the brain changes of Alzheimer's disease is likely to be much larger than the number with MCI or dementia due to Alzheimer's disease given that there is an incipient and silent (i.e., "preclinical") stage of Alzheimer's disease before the emergence of cognitive symptoms of either MCI or dementia (see Overview, page 10).<sup>249</sup> While this is still the subject of ongoing research, estimates are emerging of the prevalence of preclinical Alzheimer's disease in the population.<sup>250, 251</sup> More research is needed to validate preclinical Alzheimer's and determine how to measure it with biomarkers that conclusively represent Alzheimer's disease, as opposed to other dementia-

causing diseases. We also need to further understand if this preclinical stage is a valid representation of people who may go on to develop dementia due to Alzheimer's disease. When a conclusive connection is shown between biomarkers and the preclinical stage, and when epidemiological studies include biomarker-based diagnoses, it will be possible to estimate the number of individuals throughout the entire continuum of Alzheimer's disease (i.e., those with biomarker-confirmed Alzheimer's dementia, those with biomarker-confirmed MCI due to Alzheimer's disease and those with biomarker-confirmed preclinical Alzheimer's disease). The resulting estimated prevalence will be even higher than any estimates presented in the current report.

### **Future Facts and Figures Prevalence Estimates**

What does all this mean for future prevalence estimates? *Future Facts and Figures* reports will continue to include the estimated prevalence of individuals in the Alzheimer's dementia stage, defined according to clinical symptoms, currently estimated at 6.9 million Americans, in addition to the best available estimated prevalence of MCI due to Alzheimer's disease. Accurate, up-to-date estimates of the number of people living with these conditions will remain essential to understanding the demands on affected families, health systems, social and health safety nets, and, of course, the people living with these conditions. When biomarker-based prevalence estimates become available, *Facts and Figures* will also report the estimated prevalence of individuals with any clinical cognitive impairment and Alzheimer's disease to reflect both those in the dementia phase and those in the MCI phase of Alzheimer's. *Facts and Figures* will not include prevalence estimates of the preclinical Alzheimer's disease stage until (1) there is convincing evidence of a connection between biomarkers in this silent stage and the development of MCI due to Alzheimer's disease and (2) epidemiologic studies have estimated the number of individuals in this stage. In addition, as the evidence and epidemiological data warrant, future reports may also include estimates of the prevalence of dementia from all causes. It should be noted that both symptom-based prevalence estimates of Alzheimer's dementia and biomarker-based prevalence estimates of Alzheimer's disease are expected to increase in the future due to growth in the population of Americans age 65 and older, the group most at risk for developing cognitive symptoms.