Only a small percentage of people with early dementia eligible for new Alzheimer's drugs

August 16 2023

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Only a small percentage of older adults who are in the early stages of Alzheimer's disease meet the eligibility criteria to receive new monoclonal antibody treatments, drugs that target amyloid-ß plaques in the brain, an early sign of Alzheimer's disease.

The new research is published in *Neurology*. Clinical trial results for these drugs are only available in people in the early symptomatic stages of the disease, mild cognitive impairment or mild dementia due to Alzheimer's disease.

At the time of the study, two monoclonal antibodies called lecanemab

and aducanumab had received accelerated approval from the FDA. More recently, lecanemab, which has been shown to slow progression of the disease, has received traditional FDA approval.

"There is hope that these new therapies for Alzheimer's may slow progression of the disease for many people, although the fact remains that the drugs have only been studied in people with the earliest forms of the disease," said study author Maria Vassilaki, MD, Ph.D., of the Mayo Clinic in Rochester, Minnesota, and a member of the American Academy of Neurology.

"The inclusion and exclusion criteria of the clinical trials that led to FDA accelerated approval of these therapies form the basis of how people should be invited or discouraged from receiving one of these drugs. Our study estimates that only a small percentage of older people with early cognitive impairment due to Alzheimer's may be eligible to be treated with monoclonal antibodies for amyloid-ß in the brain."

The study included 237 people, ages 50 to 90, who had mild cognitive impairment or mild dementia, and whose brain scans showed increased amounts of amyloid-ß plaques. Researchers then looked at the eligibility criteria for clinical trials for lecanemab and aducanumab.

For lecanemab, clinical trial inclusion criteria required specific scores on a variety of thinking and memory tests, as well as a body mass index between 17 and 35. Researchers found 112 people, or 47%, would meet the inclusion criteria to participate in a clinical trial.

Then researchers looked at clinical trial exclusions, factors that could make people ineligible for a trial, including multiple health factors such as stroke, cardiovascular disease, a history of cancer, or brain scan findings that showed abnormalities like old, small brain bleeds or brain injuries due to insufficient blood supply. Researchers found that after

the exclusions, only 19 people, or 8%, would have been eligible for a lecanemab trial.

However, after modifying the exclusion criteria to include all participants with mild cognitive impairment and not applying the results of additional memory and thinking tests, 17% of participants with mild cognitive impairment would have been eligible for a trial.

For aducanumab, clinical trial inclusion criteria required specific scores on thinking and memory tests and that participants were ages 50 to 85. Researchers found 104 people, or 44%, would have met the characteristics required to participate in a clinical trial.

After further examining who would be excluded from the trial due to multiple health factors, including stroke, cardiovascular disease, uncontrolled high blood pressure, a history of cancer or brain scan findings, researchers found that only 12 people, or just 5%, would have been eligible for an aducanumab trial.

Vassilaki noted that older Black and Hispanic people have been underrepresented in clinical trials, even though they are more likely to have Alzheimer's or other dementias, and that participants in clinical trials need to represent all persons at risk for cognitive impairment.

"Our study results show only a small percentage of people with early Alzheimer's disease may be eligible to receive treatment, mostly due to chronic health conditions and brain scan abnormalities common in older adults," said Vassilaki.

"In general, clinical trial participants are healthier than the general population. Additional research is needed to examine the safety and efficacy of monoclonal antibodies targeting amyloid-ß plaques in larger, more diverse populations, as well as in less healthy populations, before

these therapies may be more widely available to people with Alzheimer's disease."

A limitation of this study was participants were primarily white. Vassilaki said that assessing these eligibility criteria in more diverse populations would be crucial.

More information: Rioghna R Pittock et al, Eligibility for Anti-Amyloid Treatment in a Population-Based Study of Cognitive Aging, *Neurology* (2023). DOI: 10.1212/WNL.0000000000207770

Matthew D Howe et al, Untangling Eligibility: Real-World Application of Anti-Beta Amyloid Monoclonal Antibodies, *Neurology* (2023). DOI: 10.1212/WNL.0000000000207873

Provided by American Academy of Neurology