Many Alzheimer's patients would not have been eligible for clinical trials of controversial new drug

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In June 2021, the Food & Drug Administration (FDA) granted accelerated approval for aducanumab to treat patients with mild

cognitive impairment or mild dementia due to Alzheimer's disease. The two phase-3 clinical trials of aducanumab on which the drug's approval was based showed increased risk of certain adverse vascular events. Though the clinical trials excluded participants based on advanced age, certain chronic diseases and use of anti-clotting medications, FDA approval was granted without contraindications or precautions for use of the drug in these patient populations.

In a research letter in *JAMA*, physician-researchers at Beth Israel Deaconess Medical Center (BIDMC) examined medical claims for Medicare enrollees with a diagnosis of either cognitive impairment, Alzheimer's disease, or Alzheimer's disease-related disorders. The team found that the vast majority of these patients had one or more conditions that would have excluded them from the aducanumab clinical trials, including cardiovascular disease, prior stroke, use of blood thinners, and age over 85 years.

"Our findings are concerning given the broad FDA labeling for aducanumab," said corresponding author Timothy S. Anderson, MD, MAS, a clinician investigator and assistant professor medicine in the Division of General Medicine at BIDMC. "The public conversation on aducanumab has focused on limited benefit and high costs, it is equally important to consider that the majority of patients with Alzheimer's disease are likely to face higher risks of adverse events than the patients studied in the trials."

Analyzing data from more than 27 million Medicare beneficiaries, Anderson and colleagues found that more than 92 percent of patients with Alzheimer's disease related dementia, 91 percent of patients with Alzheimer's disease and 85 percent of patients with cognitive impairment met at least one of the aducanumab trial exclusion criterion. More than 77 percent of patients with Alzheimer's disease related dementia met multiple exclusion criteria, as did majorities of patients

with the other diagnoses.

"Clinical trials of aducanumab studied relatively healthy participants who do not reflect the majority of older adults with dementia in the U.S.," Anderson said. "As a result, Medicare should consider restricting coverage for aducanumab to patients who meet the trial eligibility criteria, and additional clinical trials of the high-risk groups excluded from the prior trials should be required, including rigorous study of adverse events, prior to broadening coverage."

More information: Timothy S. Anderson et al, Representativeness of Participants Eligible to Be Enrolled in Clinical Trials of Aducanumab for Alzheimer Disease Compared With Medicare Beneficiaries With Alzheimer Disease and Mild Cognitive Impairment, *JAMA* (2021). DOI: 10.1001/jama.2021.15286

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