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Frequency of Biologically Defined Alzheimer Disease in Relation to Age, Sex, *APOE* ε4, and Cognitive Impairment

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Study Question

What is the degree of diagnostic agreement between biologically defined Alzheimer disease (AD) and clinically defined AD?

What Is Known and What This Paper Adds

A definitive diagnosis of AD has traditionally only been possible at autopsy, but an emerging biological research framework permits the detection of biologically defined AD in living persons. This investigation's results provide evidence for strong but incomplete agreement between the biological and clinical definitions of AD.

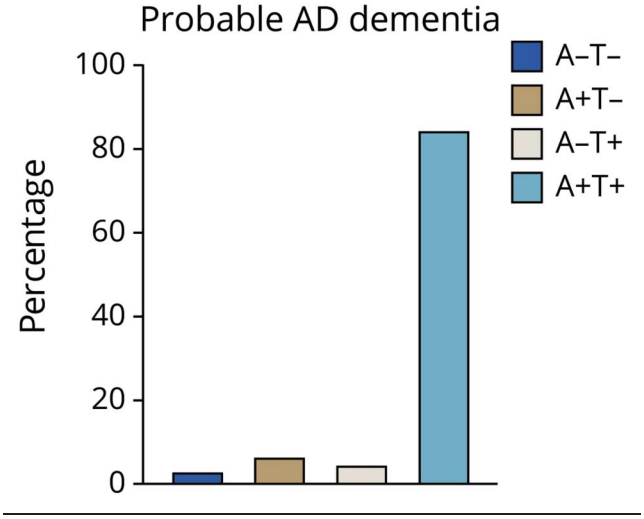
Methods

For this diagnostic test study, the investigators analyzed data from 305 older adults who participated in the Translational Biomarkers for Aging and Dementia study, which occurred through the McGill University in Montréal. Clinicians blinded to neuroimaging data used clinical features to classify the selected participants as being cognitively unimpaired (CU; n = 166) or as having amnestic mild cognitive impairment (n = 77) or probable AD dementia (n = 62). These older adults underwent amyloid-β (Aβ) PET scans with [^{18}F]-AZD4694 and tau PET scans with [^{18}F]-MK6240. The investigators defined Aβ-positivity (i.e., A+ status) as having an [^{18}F]-AZD4694 standardized uptake value ratio (SUVR) ≥1.55 across the neocortex, and they defined tau-positivity (i.e., T+ status) as having an [^{18}F]-MK6240 SUVR ≥1.24 in a composite of temporal cortical regions. They defined biological AD as being A+T+, in line with the recent framework from the National Institute of Aging-Alzheimer's Association (NIA-AA). The primary outcome was the degree of overlap between cohort members meeting the biological definition of AD and those meeting the clinical definition of AD.

Results and Study Limitations

The investigators found strong agreement between the biological and clinical definitions of AD, with the 85.2% of people who met the clinical definition of AD also meeting the biological definition. Furthermore, 7.9% of people in the CU group met the biological definition of AD. These findings are Class I evidence for strong agreement between the biological and clinical definitions of AD. The present study's limitations include the sensitivity–specificity tradeoffs inherent to biomarker dichotomization and the study's focus on a recruited cohort, which may limit generalizability to the broader population.

Figure Percentages of People With Clinically-Defined Probable AD Dementia Who Were A − T− (Dark Blue), A+T− (Brown), A − T+ (Gray), and A+T+ (Light Blue)



Study Funding and Competing Interests

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A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The corresponding author(s) of the full-length article and the journal editors edited and approved the final version.

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