was associated in older APOE-ε4 noncarriers. Conversely, amyloid positivity increased with age in patients with frontotemporal dementia, vascular dementia, and dementia with Lewy bodies, suggesting, as the authors mention, that amyloid is present as secondary pathology and the clinical syndrome is driven by non-AD pathologies.

Jansen et al1 and Ossenkoppele et al2 provide succinct meta-analyses of considerable clinical value. Persons without dementia have an increasing prevalence of cerebral amyloid pathology with age, APOE genotype, and cognitive loss as measured by PET imaging or CSF findings. Similarly, among persons with dementia, the prevalence of amyloid pathology was related to clinical diagnosis, age, and APOE genotype. Together, these data show the immense potential clinical use of amyloid imaging to make the correct diagnosis in early-onset dementia and, more specifically, to establish the diagnosis of AD-type dementia and noncarrier APOE-ε4 genotype among persons older than 70 years.

Immunotherapeutics are now at a critical juncture, with clinical trials currently evaluating several anti–amyloid-β monoclonal antibodies in asymptomatic individuals who are at risk for AD by virtue of having positive findings on PET amyloid imaging (NCT01998841, NCT00869817, and NCT02008357). If passive monoclonal therapy can be shown to have clinical benefit by delaying or preventing dementia due to AD, it will be a major achievement. Additional clinical trials with other immunotherapies, including active vaccination generating anti–amyloid-β antibodies using a DNA Aβ39 vaccine9 or other immune strategies,10 will then be developed and implemented. The meta-analyses reported here1-4 provide the basis for clarifying the parameters for using anti–amyloid-β therapies among patients at risk for AD and providing impressions as to which patients are most at risk and would potentially benefit most with anti–amyloid-β therapy.


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Several concerns have been raised about the study conduct, integrity, and scientific validity involving an article published in JAMA by Dr Sato et al.1 After communicating these concerns to the author and evaluating his response, we have contacted administrative officials at the author’s institution and requested that they conduct an investigation to evaluate the scientific integrity of the research and the validity of the reported study results. This notice of concern is to inform readers about these possible issues related to this article. After additional information from this investigation becomes available, we will determine whether additional action is warranted.

REFERENCE