Statement on Alzheimer's & Dementia® Journal Publication about Association between Reduction of Amyloid Beta and Slowing of Cognitive and Functional Decline in Alzheimer's Disease

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Today, *Alzheimer's & Dementia: The Journal of the Alzheimer's Association* published an updated meta-analysis demonstrating a likely causal association between removal of amyloid beta plaques in the brain and slower cognitive and functional decline in Alzheimer's disease. These findings suggest that amyloid beta plaque remains a viable biological target for the prevention and treatment of Alzheimer's disease.

The results are based on updates to a meta-analysis published in the British Medical Journal (BMJ) on February 25, 2021, which had concluded that reduction in amyloid levels alone was unlikely to substantially slow cognitive decline within the follow-up period of most typical trials. The original authors created a web interface with an interactive version of their analysis to encourage updates and recalculations from other researchers. The updated meta-analysis published today used the same methodology as the original with the addition of two new clinical trials into the analysis.

"The totality of the updates to the analysis led to the finding of a causal association between removal of amyloid beta plaques in the brain and slower cognitive decline on all endpoints assessed, an intriguing contrast to the original findings," said study co-author, Robert Platt, PhD, Professor and Albert Boehringer Chair, McGill University, Departments of Epidemiology, Biostatistics, and Occupational Health and of Pediatrics. "We hope this work can continue to evolve and inform clinical development and help advance the field of Alzheimer's research as a whole."

Removal of amyloid beta was measured via positron emission tomography (PET) with standardized uptake value ratio (PET-SUVR). The effect of amyloid beta removal on cognitive and functional decline was statistically significant across all endpoints evaluated in the original analysis: Clinical Dementia Rating–Sum of Boxes (CDR-SB), Alzheimer's Disease Assessment Scale–Cognitive Subscale (ADAS-Cog), and Mini-Mental State Examination (MMSE).

The complete publication titled, "Effect of reduction in brain amyloid levels on change in cognitive and functional decline in randomized clinical trials: an instrumental variable meta-analysis" is available on the website of the *Alzheimer's & Dementia Journal* .